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CLINICAL INVESTIGATION.(U)
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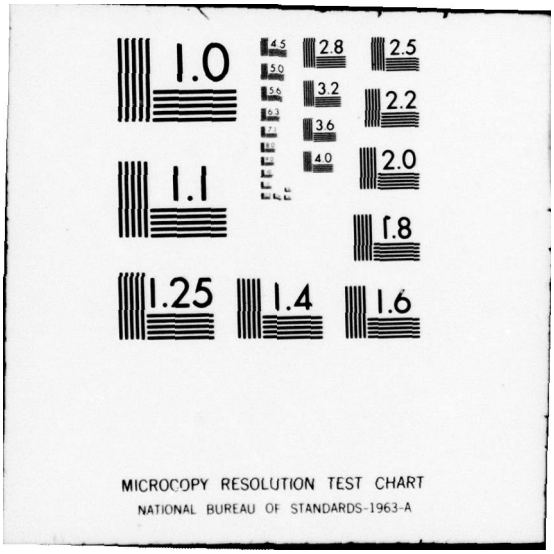
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Clinical Investigation Service

Annual Progress Report

30 September 1977

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The findings of subject report are not to be construed as an official Department of the Army position unless so designated by other authorized documents.

19. KEY WORDS (Continue on reverse side if necessary and identify by block number)

Clinical Investigations, all medical specialties
experimental projects (planning, coordination, staff supervision, execution, review and monitoring)
research protocols
in-house research (continued on reverse side)

20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

Subject report identifies the research activities conducted by Fitzsimons Army Medical Center investigators through protocols approved by the Clinical Investigation Committee and registered with the Clinical Investigation Service during Fiscal Year 1977 and other known presentations and publications by the Fitzsimons Army Medical Center professional staff. The research protocols described were conducted under the provisions of AR 40-38, as amended, Clinical Investigation Program, AR 40-7, Use of Investigational Drugs in Humans, (continued on reverse side)

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Block 19. Key Words

publications, presentations of research data (at national, international and regional science meetings)
post graduate educational programs
protocol training and support programs
protocol registration
protocol status (ongoing, completed, terminated)
technological base (personnel and equipment)
experimental design (statistical tools, etc.)

Block 20. Abstract

AR 70-25, Use of Volunteers as Subjects of Research and FAMC Reg. 40-38, Clinical Investigation Service, Policies and Procedures, to insure the medical being, preservation of rights and dignity of human subjects who participated in these investigations.

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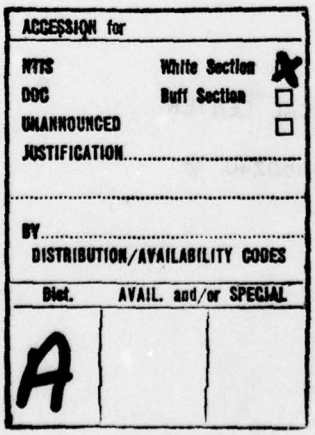

CLINICAL INVESTIGATION PROGRAM

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ANNUAL PROGRESS REPORT

30 SEPTEMBER 1977

CLINICAL INVESTIGATIONS (U)

FITZSIMONS ARMY MEDICAL CENTER

DENVER, COLORADO 80240

FOREWORD

This report identifies the research activities conducted by Fitzsimons Army Medical Center investigators through protocols approved by the Clinical Investigation Committee and Human Use Committee and registered with the Clinical Investigation Service during Fiscal Year 1977 along with other known presentations and publications by FAMC professional staff.

The research protocols described in this report were conducted under the provisions of AR 40-38, as amended*, Clinical Investigation Program, AR 40-7, Use of Investigational Drugs in Humans, AR 70-25, Use of Volunteers as Subjects of Research, and FAMC Reg. 40-8, Clinical Investigation Program, FAMC, to insure the medical safety, well being, preservation of rights and dignity of human subjects who participated in these investigations.

In conducting the research described in this report, the investigator(s) adhered to AR 70-18, Laboratory Animals, Procurement, Transportation, Use, Care, and Public Affairs and the "Guide for Laboratory Animal Facilities and Care," as promulgated by the Committee or the Guide for Laboratory Animal Resources, National Academy of Sciences, National Research Council.

Clinical Investigation Service is especially grateful to MAJOR GENERAL Kenneth R. Dirks, MC, Commanding General, Fitzsimons Army Medical Center, his professional and administrative staffs, and to the Commanding Officers and staffs of other supporting activities for the cooperation and assistance provided the Clinical Investigation Service in our efforts to accomplish our mission. Finally, I would like to recognize the outstanding work, dedication, and whole-hearted corroboration of my entire staff. I would especially like to thank my Protocol and Editorial Assistant, Mrs. Val McCrill and Mrs. Chris Montoya, clerk-stenographer, without whose assistance and support this report would not have been possible.

Donald G Corby

DONALD G. CORBY, M.D.
COL, MC
Chief, Clinical Investigation Service

*Reference AR 40-38, para 6, and interim change thereto: DA message R 151530 Z Jul, 75 -- DA (TSG) WASH DC // DASG-ZA SGRD-HR // and change thereto (DA message 122044Z Sep 75, ofc ref as cited), effective 1 Jan 76.

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PRESENTATIONS

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Stein, M.R.: Laboratory Evidence of Immune Complexes in Patients on Hyposensitization Therapy. Presented: American Congress of Allergy and Immunology, New York, New York, March 1977.

Posey, W.C.: The Effects of Therapeutic Doses of Corticosteroids on Immunoglobulin Levels. Presented: 5th Annual Meeting, Association of Military Allergists, Denver, Colorado, September 1976.

Nelson, H.S.: Intensive Immunotherapy. Daily Administration of Allergy Extracts to Atopic Individuals. Presented: 5th Annual Meeting, Association of Military Allergists, Denver, Colorado, September 1976.

Stein, M.R.: Use of Histamines as a Positive Skin Test Control. Presented: 5th Annual Meeting, Association of Military Allergists, Denver, Colorado, September 1976.

Pfeutze, B.: A Controlled Study of Animal Dander in Immunotherapy. Presented: 5th Annual Meeting, Association of Military Allergists, Denver, Colorado, September 1976.

Nelson, H.S.: In Search of the IgE Reagin. Presented: 5th Annual Meeting, Association of Military Allergists, Denver, Colorado, September 1976.

Posey, W.C.: The Effects of Corticosteroids on Immunoglobulin Levels. Presented: American Congress of Allergy and Immunology, New York, New York, March 1977.

Nelson, H.S.: The Importance of IgG Short Term Skin Sensitizing Antibodies in Clinical Allergy. Presented: 72nd Annual Meeting, American Thoracic Society, San Francisco, California, May 1977.

Stein, M.R.: Monitoring Aspiration by Isotope Techniques. Presented: 6th Annual Meeting, Association of Military Allergists, Denver, Colorado, September 1977.

Allergy - continued

Weber, R.W.: Effect of Theophylline on Lower Esophageal Sphincter Pressure. Presented: 6th Annual Meeting, Association of Military Allergists, Denver, Colorado, September 1977.

Mansfield, L.E.: Pulmonary Response in Asthmatics to Intraesophageal Installation of Hydrochloric Acid. Presented: 6th Annual Meeting, Association of Military Allergists, Denver, Colorado, September 1977.

McDonnell, J.T.: Bronchodilation and Bronchoconstriction Induced by Exercise in Asthmatics. Presented: 6th Annual Meeting, Association of Military Allergists, Denver, Colorado, September 1977.

Weber, R.W.: Evaluation of Clinical Importance and Cross Allergenicity in the Chenopod-Amaranth Families. Presented: 6th Annual Meeting, Association of Military Allergists, Denver, Colorado, September 1977.

Nelson, H.S.: Studies on the Effect of Diluents and Preservatives on Extract Stability. Presented: 6th Annual Meeting, Association of Military Allergists, Denver, Colorado, September 1977.

Mansfield, L.M.: Measurement of Total Respiratory Resistence by Forced Oscillation in Children Ages 3-5. Presented: First Prize, Hugh Mahon Lectureship Award, June 1977.

Cardiology

Thomas, H.M., and Way, G.L.: Contrast Echocardiography - A Method to Augment Diagnostic Accuracy of M-Mode Echocardiography. Presented: Sixth Annual Army Association of Cardiology Meeting, WBAMC, El Paso, Texas, 1977.

Way, G.L.: The Natural History of Hypertrophic Cardiomyopathies in Infants of Diabetic Mothers. Presented: Sixth Annual Army Association of Cardiology Meeting, WBAMC, El Paso, Texas, 1977.

Boland, M.J., Kleiner, J.P., and Brundage, B.H.: The Markedly Positive Stress Test - An Indicator of Left Main Coronary Artery Disease. Presented: Sixth Annual Army Association of Cardiology Meeting, WBAMC, El Paso, Texas, 1977.

Way, G.L.: Medical Management of Severe Systemic Hypertension in Infants with Isolated Coarctation of the Aorta. Presented: American Academy of Pediatrics, 46th Annual Meeting, New York, New York, 1977.

Cardiology - continued

Way, G.L.: Symptomatic High Altitude Pulmonary Hypertension and Cor Pulmonale in Infancy. Presented: American Academy of Pediatrics, 46th Annual Meeting, New York, New York, 1977.

Dermatology

Nuss, D.D.: Herpes Simplex, Herpes Zoster. Presented: University of Colorado Medical Center Family Practice Post Graduate Course, 1977.

Aeling, J.L.: Deep Fungal Infections. Presented: University of Colorado Aspen Summer Skin Seminar, Aspen, Colorado, 1977.

Endocrinology

Hofeldt, F.D.: The Problems of Hypoglycemia. Presented: Minnesota Academy of Family Physicians, Detroit Lakes, Minnesota, August 1976.

Hofeldt, F.D.: Reactive Hypoglycemia - Current Concepts of Diagnosis and Therapy. Presented: Diabetes Symposium, American Diabetes Association of Minnesota, Thief River Falls, Minnesota, 1977.

Hofeldt, F.D.: Reactive Hypoglycemia. Presented: 1976 Symposium on Diabetes Mellitus, Mankato, Minnesota, October 1976.

Treece, G.L.: The Endocrine Pancreas. Presented. Colorado Chapter of Medical Technicians, Fitzsimons Army Medical Center, Denver, Colorado, November, 1977.

Gastroenterology

Gremillion, D.E.: Biliary Obstruction, A Complication of Chronic Pancreatitis Diagnosed by Endoscopic Retrograde Cholangiopancreatography (ERCP). Presented: Southern Medical Association Meeting, Division on Gastroenterology, New Orleans, Louisiana, November 1976.

CLINICAL INVESTIGATION SERVICE

Corby, D.G.: Evaluation of Cyclo-Oxygenase Pathway in Platelets of the Newborn. Presented VI Internation Congress on Thrombosis and Hemostasis, Philadelphia, Pennsylvania, 1977.

Charles, M.A.: Activation of m-RNA for CaBP by 1,25-D_3. Presented: Clinical Research, Carmel, California, 1977.

Clinical Investigation Service - continued

Brown, G.L., Tull, A.H., Calcagno, J.V., Cromwell, R.K., Bennett, D.E., Spaulding, H.S., and W.A. Todd: Incidence of Group A Beta-Hemolytic Streptococcus in Healthy Children. Presented: American Society for Microbiology, New Orleans, Louisiana, May 1977.

Kolb, J.G., Rothlauf, M.V., and G.L. Brown: Isolation of Mycobacterium kansasii on Mitchison's Selective 7H11 Medium. Presented: American Society for Microbiology, New Orleans, Louisiana, May 1977.

Brown, G.L.: Laboratory Parameters in Serum Gammopathies: Serum Protein Profiles. Presented: Colorado State University, Boulder, Colorado, June 1977.

PEDIATRICS

Squire, E.N.: Neonatal Sepsis. Presented: 12th Annual Uniformed Services Pediatric Seminar, El Paso, Texas, 1977

Squire, E.N: Neonatal Sepsis. Presented: WSPR, Carmel, California, 1977.

PSYCHIATRY

Rabin, R.A.: A Proposed New Model for Training Pediatric Residents in the Psychosocial Aspects of Pediatrics. Presented: American Academy of Child Psychiatry, Houston, Texas, 1977.

PATHOLOGY

Glenn, G.C.: Urine Chemistry - A New CAP Survey Program. Presented: CAP Fall Meeting, 1976.

Glenn, G.C., and Hathaway, T.K.: Urine Chemistry - A New CAP Survey Program. Presented: CAP Spring Meeting, 1977.

SURGERY

Orthopedic Service

Eversmann, W.W.: Fractures and Dislocations of the Hand. Presented: Orthopedics for the Family Physician, Aspen, Colorado, 1977.

Eversmann, E.W.: Dislocation of Phalanges. Presented: International Hand Surgery Symposium, Vail, Colorado, 1977.

Eversmann, W.W.: Extensor Mechanism Injury in the Digits. Presented: International Hand Surgery Symposium, Vail, Colorado, 1977.

Orthopedic Service - continued

Eversmann, W.W.: Metacarpophalangeal Joints in Rheumatoid Disease. Presented: International Hand Surgery Symposium, Vail, Colorado, 1977.

Eversmann, W.W.: Principles of Upper Extremity Rehabilitation. Presented: International Hand Surgery Symposium, Vail, Colorado, 1977.

Eversmann, W.W.: Injuries to the Hand in Children. Presented: Orthopedic Nurses Symposium, Denver, Colorado, December 1976.

Eversmann, W.W.: Extensor Tendon Injuries to the Digits. Presented: International Hand Surgery Symposium, Vail, Colorado, August 1976.

Eversmann, W.W.: Initial Care of the Mangled Hand, Fractures of the Hand in Children, Hand Infections, Hand Fractures in Children, Upper Extremity Prosthetics, Challenging Case Presentations, Recent Concepts in Compression Neuropathy, Basic Photography for the Hand Surgeon, Indications for Open Reduction of Metacarpal Fractures. Presented: University of Colorado Medical Center Hand Seminar, Denver, Colorado, 1977.

Eversmann, W.W.: Hand Infections. Presented: Children's Orthopedics Symposium, Denver, Colorado, 1977.

Goldberg, B.: Radiofrequency Rhizotomy. Presented: Back Symposium, Denver, Colorado, 1977.

Sulkosky, J.: Three Bone Forearm: A Salvage Procedure for Treatment of Ulnar Nonunion, Infection and Tumors. Presented: Society of Military Orthopedic Surgeons, Silver Springs, Maryland, November 1976.

Ballard, A.: Treatment of Femoral Fractures. Presented: Orthopedic Nurses Symposium, Denver, Colorado, December 1976.

Ballard, A.: Treatment of Epiphyseal Injuries in Children. Presented: Orthopedic Nurses Symposium, Denver, Colorado, December 1976.

Ballard, A.: Traumatic Patellar Dislocations. Treatment of Wounds of the Lower Extremity. Operative Treatment of Slipped Capital Femoral Epiphysis. Presented: University of Utah, Salt Lake City, Utah, 1977.

Ballard, A.: Sprains, Strains, and Contusions. Common Problems of the Lower Extremity in Children. Fractures of the Upper Extremity in Children. Evaluation and Treatment of Clubfeet. Presented: Orthopedics for the Family Physician, Aspen, Colorado, 1977.

Orthopedics - continued

Ballard, A.: Slipped Capital Femoral Epiphysis. Congenital Dislocated Hip. Reconstruction of the Knee. Evaluation of Scoliosis. Nonoperative Treatment of Scoliosis. Operative Treatment of Scoliosis. Clubfoot Evaluation and Treatment. Presented: Triper Army Medical Center, Hawaii, September 1977.

Ophthalmology

Bode, D.D.: Occipital Neuritis. Presented: Colorado Ophthalmological Society, Spring Meeting, 1977.

Manson, R.A.: Transient Visual Loss. Presented: Colorado Ophthalmological Society, Spring Meeting, 1977.

Thoracic and Cardiovascular Surgery Service

Barry, M.J.: Carcinoma of the Lung. Presented: 28th Annual Symposium of Pulmonary Disease, Fitzsimons Army Medical Center, Denver, Colorado, September 1976.

Barry, M.J.: Anatomy of a Malpractice Suit. Presented: Annual Meeting of Army Association of Cardiologists, El Paso, Texas, May 1977.

Otolaryngology Service

Zajtchuk, J.T.: Hypercoagulability as a Cause of Sudden Hearing Loss. Presented: XV Pan American Congress, New Orleans, Louisiana, November 1976.

Krekorian, E.A.: Infections of the Head and Neck. Presented: 62nd Clinical Congress of the American College of Surgeons, Chicago, Illinois, 1977.

Plastic Surgery Service

Rich, J.D.: Reconstruction of Hair-Bearing Facial Features. Presented: Symposium of Military Plastic Surgeons, WRAMC, Washington, D.C., January 1977.

Cullington, J.R.: Massive Abdominal Wall Defects. Presented: Symposium of Military Plastic Surgeons, WRAMC, Washington, D.C., January 1977.

Zbylski, J.R.: Correction of Lower Eyelid Ptosis with an Autogenous Ear Cartilage Graft. Presented: American Association of Plastic Surgeons, Chicago, Illinois May 1977.

Urology Service

Dobbs, R.M.: Angiomyolipoma Associated with Tuberosclerosis.
Presented: South Central Section AUA Meeting, San Antoino, Texas
1977.

Buntley, D.W.: Pyo-Ureter Masquerading as Post-Appendectomy Abscess.
Presented: Society of University Urology Residents Meeting,
Chicago, Illinois, 1977.

UNIT SUMMARY SHEET

UNIT SUMMARY SHEET

Clinical Investigation Program, FAMC

Clinical Investigation efforts by FAMC personnel in FY 77 culminated in the publication of 116 articles and 67 presentations and lectures at national, international, and regional scientific meetings. As of 30 September 1977, there were 107 research protocols on the CIS register. Of these 64 projects were ongoing and 43 new registrations.

Objectives: To encourage the performance of clinical investigations by AMEDD personnel, especially by personnel assigned to Army hospitals where post graduate educational programs are conducted. To aid in the planning, development, support, and execution of experimental clinical studies, both in patients and by directly related laboratory work, into clinical problems of significant concern in the necessary health care of members of the military community. To provide the physician experience in research and investigative procedures. To provide a base for continued training in such organized inquiries for those personnel who will become teaching chiefs and medical consultants in the Army Medical Department.

Technical Approach: Provides direction, management, and support as outlined under provisions of AR 40-38, as amended, Clinical Investigation Program; AR 40-7, Use of Investigational Drugs in Humans; AR 7025, Use of Volunteers as Subjects of Research, and MCR 40-8, Clinical Investigation Service, FAMC. Provides guidance, assistance, and support to the Center staff in matters pertaining to the program. Coordinates the FAMC program with higher headquarters and other facilities.

Manpower: Current and authorized strength is outlined.

Description	Grade	MOS	Br	Auth	Actual	Name
C, Clin Rsch	06	60P9B	MC	1	1	Corby
C, Immuno Sec	05	68A9A	MS	1	1	Brown
Internist	05	61F9C	MC	0	1	Charles
Lab Admin	03	68F00	MS	1	1	Marsteller
C, Surg - Rsch Labs	03	64F9D	VC	1	1	Hofmann
C, Micro Sec	04	68A00	MS	1	1	Damato
Physiologist-PhD	03	68J00	MS	1	0	
Biochem	03	68C00	MS	1	0	
Microbiologist	03	68A00	MS	0	1	Quigg
NCOIC	E7	92B4R		1	1	Underhill
C. Med Lab NCO	E7	92B4R		1	1	Engle
SR O.R. SP	E6	91D3R		1	1	Smith, N.
Bio Sci Asst	E6	01H20		3	3	Glab

Description	Grade	MOS	Br	Auth	Actual	Name
Bio Sci Asst	E5	01H20		1	1	Andersen
Bio Sci Asst	E3	01H20		1	1	Gallegos
Bio Sci Asst	E4	01H20		1	1	Foster
Vet Sp	E5	91T2R		NTD	1	Rich
O.R. Sp	E6	91T2R		NTD	1	Smith, J.
Microbiol-PhD	13	0403 GS		1	1	O'Barr
Microbiol	09	0403 GS		3	3	Lima Rothlauf Tull
Med Technol	09	0644 GS		1	1	Rush
Biochem	09	1320 GS		1	1	Swanson
Microbiol	07	0403 GS		6	6	Cromwell Rangel Kile Morse LeDoux Paine
Rsch Chem	07	1320 GS		3	2	McNamara Noble
Bio Lab Tech	07	0404 GS		1	1	Hakes
Animal Tech	05	0404 GS		1	1	Mercill
Protocol Asst	06	0318 GS		1	1	McCrill
Animal Caretaker	05	7706 WG		2	2	Beltran Hitchcock
Clerk-Steno	04	0318 GS		1	1	Montoya

	FY-76 Program	FY-77 Program	FY-78 Program
Civilian Pay	329,374	382,810	356,100
Travel	2,572	3,856	3,851
Supplies	115,000	158,153	156,075
Equipment	85,000	80,000	23,000
Contracts	29,000	20,029	21,800
Other (Military)		267,269	219,686

PROGRESS:

In order to comply with the mission directives as outlined in AR 40-38, as amended, Clinical Investigation Program and FAMC 40-8, an aggressive and comprehensive program of expansion of the Clinical Investigation Service, FAMC, has been undertaken. The TDA has been redesigned to facilitate lines of command, coordination between sections, and better utilization of personnel and facilities. This reorganization has resulted in an integrated administrative section (Office of the Chief) and five independent functional laboratory sections: Immunology, Microbiology, Biochemistry, Surgical Research Laboratories and the Coagulation Laboratory. All sections are fully staffed, equipped and are presently providing technical support for registered protocols and teaching programs.

Immunology Section

During FY 77 the Immunology Section, in addition to on-going research investigations, provided consultative services for patients in the areas of cellular and humoral immunology, hemoglobinopathies and serum gammopathy differentiation. The facilities of the section were also made available for immunology laboratory training to residents in fellowship training in Adult and Pediatric Allergy. This training followed three instructional phases: Laboratory procedures in immunology and immuno-chemistry as applicable to clinical medicine, characterization of serum globulins and leukocyte studies as applicable to immunologic disorders, and neutrophil functional studies. During this period, this section also provided training for HSC approved DAC training in microbiology for two (2) civilians. Two new procedures were evaluated and are currently in use: Neutrophil chemiluminescence and neutrophil chemotaxis using the C^{5f} system.

Microbiology Section

Two independent subsections of the Microbiology Section, CIS provide technical support for on-going protocols, training and consultative services:

Medical Microbiology Subsection:

Provides support for research studies requiring isolation and identification of pathogenic micro-organisms, development of new isolation media and culture collection systems. Current

capabilities include: Isolation and identification of Group B and Group B beta hemolytic streptococcus including definitive serologic grouping and sub-typing, potential pathogens of the upper respiratory tract, mycoplasma, ureaplasma and L-forms.

Mycobacteriology Subsection:

Historically, Fitzsimons Army Medical Center has provided leadership in the identification and treatment of tuberculosis in the military community. In accordance with the commanders' directives, CIS provides mycobacteriology (TB) support (processing clinical specimens and reference cultures) to the listed MEDDACS. The unique ongoing computer storage and analyses of mycobacteriologic data from tuberculin patients used for laboratory follow-up patients' specimens, quality control and analyses of clinical data provides clinical support not found in any other USA MEDD laboratory. Additional indepth mycobacterial studies on patients; i.e., serum drug levels, serum inhibition tests, identification of mycobacteria other than M. tuberculosis are also provided.

MEDDACS receiving support are:

Ft. Carson	Letterman AMC	Scott AFB
Ft. Leavenworth	Tripler AMC	Air Forces Bases located
Ft. McPherson	Madigan AMC	at: Baker's Field, CA
Ft. Ord		Minot, S. Dak.
Ft. Riley		
Ft. Sill		

In addition, TB reference laboratory support is accorded: Communicable Disease Center, Atlanta, GA., PHS, Pine Ridge Reservation, S.D.

Biochemistry Section:

The Biochemistry Section, CIS has assumed the responsibility of providing those radioimmunoassays and workloads formerly accomplished by the Metabolic Division, LAIR. The bulk of these assays involves endocrinology studies (steroids, growth hormones, insulin, thyroid functions, etc) and constitutes a substantial increase in total workload and costs.

Surgical Research Laboratories Section:

The Surgical Research Laboratories Section, CIS has greatly expanded its services. In addition to providing several training programs, this activity has significantly expanded its support to encompass a second

operating room facility, upgrading of X-ray and physiological monitoring equipment. The increased surgical workload has resulted from support given to protocols dealing with cardiovascular research, vena caval, and renal transplants.

Coagulation Laboratory Section:

The Coagulation Laboratory Section, CIS, provides laboratory support for the study of hemostatic conditions, techniques for investigating the various parameters of the clotting mechanisms, and research into platelet function of newborns. In addition, this section provides timely and necessary assistance to the Coagulation Laboratory of the Department of Pathology, FAMC.

CIS received from HSC two civilian microbiology intern training positions. This program brings in a qualified aspirant at the GS-05 entrance level and upon successful completion of a rigorous training program allows for non-competitive promotion to GS-07 and finally the GS-09 journeyman level. Currently, both of the two assigned interns have successfully completed phase I and have been promoted.

CIS has acquired a new mission requirement, that of becoming accredited by the College of American Pathologists (CAP). This accreditation is a requirement of the Commander's Laboratories as directed by HSC. Accordingly, CIS has initiated the appropriate administrative procedures.

An urgent minor construction request for an Animal Care Facility including surgical and x-ray capabilities and costing approximately $399,000 has received both local and HSC approval and is currently being staffed through OTSG for The Surgeon General's signature. This facility will fulfill all standards of accreditation for Animal Care (AAACAC) and AR 70-18, Laboratory Animals, Procurement, Transportation, Use, Care, and Public Affairs.

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DETAIL SHEETS

MEDICINE

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Tuberculosis Research Follow-up Program.

WORK UNIT NO: 67/100

PRINCIPAL INVESTIGATOR: Roald A. Nelson, COL, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To facilitate proper collection of research records of tuberculosis patients and to provide a central repository for all such records. (Procedural Guide, Number 40-957, dated 27 May 1957).

TECHNICAL APPROACH

All patients admitted to the Tuberculosis Service have research files made which include representative x-rays, clinical summaries, bacteriology printouts of smear and culture data and any other records deemed appropriate for the individual case. These files are expanded when follow-up x-rays, reports and cultural data are obtained from our own clinic follow-up or from other hospitals. The information obtained is used to analyze various aspects of clinical tuberculosis, treatment results, and specific types of tuberculosis.

Manpower (in professional man years): 0.2/yr

Funding (in thousands)	FY 76:	4.0
	FY 77:	4.0

PROGRESS

This project has to date accumulated detailed information on over 25,000 patients with tuberculosis. It is most assuredly the best file of its type in the United States and will continue to contribute significantly to future data computations and papers in the field of clinical tuberculosis.

WORK UNIT 67/100

PROGRESS - continued

The modern concepts of therapy for tuberculosis stem from data such as we have in this file. These concepts include short-term hospitalization for treatment of active tuberculosis, early discharge from follow-up after medical therapy, frequency of pleural tuberculosis in young adults with pleural effusion and positive skin tests, and the incidence of extra pulmonary tuberculosis in the population of tuberculosis infected individuals.

Publications:

(1) Christensen, W. I.: Genitourinary Tuberculosis: Review of 102 Cases. Medicine 53:377, 1974.

(2) Buchanan, B. D.: Atypical Tuberculosis Due to Type I and Type III Atypical Mycobacteria. (Submitted for Publication).

(3) Gerace, J., Nelson, R. A.: Incidence of Drugs Resistant Tuberculosis in Oriental Females Treated at Fitzsimons Army Medical Center and Scott Air Force Base Medical Center. (In preparation.)

Presentations:

(1) Christensen, W. I.: Genitourinary Tuberculosis at FAMC from 1961 to present. Presented: 25th Annual Pulmonary Disease Symposium, Fitzsimons Army Medical Center, Denver, Colorado, September 1972.

(2) Christensen, W. I.: Genitourinary Tuberculosis at FAMC from 1961 to present. Presented: Regional American College of Physicians Meeting. Colorado Springs, Colorado, January 1973.

(3) Christensen, W. I.: Genitourinary Tuberculosis at FAMC from 1961 to present. Presented: Hugh Mahon Lectureship Award Competition, Fitzsimons Army Medical Center, Denver, Colorado, May 1973 (submitted as research paper).

(4) Christensen, W. I.: Drug Resistant Tuberculosis from Vietnam. Presented: 25th Annual Pulmonary Disease Symposium, Fitzsimons Army Medical Center, Denver, Colorado, September 1972.

(5) Nelson, R. A.: Tuberculosis of the Spine (Potts' Disease). Presented J. J. Waring Chest Conference. Estes Park, Colorado, August 1974.

WORK UNIT 67/100

PROGRESS - continued

(6) Nelson, R. A.: Pleural and Lymph Node Tuberculosis: Presented at the Course Clinical Management and Control of Tuberculosis. Presented three times yearly by National Jewish Hospital, Denver, Colorado.

(7) Buchanan, B.: Atypical Tuberculosis. Presented: 28th Annual Pulmonary Disease Symposium, Fitzsimons Army Medical Center, Denver, Colorado, September 1975.

(8) Nelson, R. A.: Extra Pulmonary Tuberculosis. Presented: Fitzsimons Army Medical Center, Denver, Colorado, September 1975.

(9) Christensen, W.I.: Genitourinary Tuberculosis. Presented: At the course, Clinical Management and Control of Tuberculosis. Sponsored by National Jewish Hospital, Denver, Colorado, three times yearly.

(10) Gerace, J., Nelson, R.A., Byrd, R.: Drug Resistant Tuberculosis in Oriental Females. Presented: Annual Meeting of American Thoracic Society, San Francisco, California, May 1977.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: A Controlled Clinical and Laboratory Evaluation of Co-Seasonal Injection Therapy in the Treatment of Allergic Rhinitis and Asthma.

WORK UNIT NO.: 73/117

PRINCIPAL INVESTIGATOR: Harold S. Nelson, COL, MC

ASSOCIATE INVESTIGATOR: T. P. O'Barr, Ph.D., DAC

OBJECTIVES

To assess the feasibility of the daily administration of allergy extract and to assess the immunologic response to the daily immunotherapy in comparison with normal weekly injection program.

TECHNICAL APPROACH

Patients with seasonal allergic rhinitis who are seen either while symptomatic or shortly prior to periods of anticipated seasonal symptoms are selected for study. Allergy extracts are administered on a daily basis. The immunologic response to this daily injection therapy was monitored by serum RAST and blocking antibody titers.

Manpower (in professional man years): 0.02/yr

Funding (in thousands) FY 76: 2.0
FY 77: 0.6

PROGRESS

Approximately thirty-six patients received daily injections of allergy extract. The specific IgE response to this immunotherapy was determined by RAST. Attempts to measure blocking antibody were made using a double antibody technique but the results were technically unsatisfactory, probably due to the high percentage of clinically non-relevant proteins in the allergy extract employed.

WORK UNIT NO.: 73/117

PROGRESS - continued

Publications:

(1) Nelson, H.S., and Posey, W.C.: Intensive Immunotherapy: Daily Administration of Allergy Extracts to Atopic Individuals. Proceedings of the 5th Annual Meeting Association of Military Allergists, p. 52, 1976.

Presentations:

(1) Nelson, H.S.: Intenstive Immunotherapy: Daily Administration of Allergy Extracts to Atopic Individuals. 5th Annual Meeting Association of Military Allergists, Fitzsimons Army Medical Center, Denver, Colorado, September 22, 1976.

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Active Antigens in House Dust.

WORK UNIT NO.: 73/135

PRINCIPAL INVESTIGATOR: Lyndon E. Mansfield, MAJ, MC

ASSOCIATE INVESTIGATOR: Harold S. Nelson, COL, MC

OBJECTIVES

To determine to what degree the reactivity of house dust extract is related to its contents of cat dander, dog dander, mite products and cotton degeneration products.

TECHNICAL APPROACH

The contribution to the antigenicity of house dust by the identifiable components of cat dander, dog dander, house dust mite, antigen and antigens derived from the degeneration of cotton will be analyzed by several immunological approaches. This will include the ability of the individual components to neutralize the RAST reaction of house dust allergic serum against house dust antigen disks. The ability of the same components to block the past hemogluttination test to house dust, then the ability of immuno adsorbents made from antisera to these individual components to remove activity from house dust extract.

Manpower (in professional man years): 0.2/yr

Funding (in thousands) FY 76: 0
FY 77: 2.0

PROGRESS

During this reporting period, rabbits have been injected with extracts of cat and dog dander, house dust mite and aged cotton fibers. Thus

WORK UNIT NO.: 73/135

PROGRESS - continued

successful antisera have been raised against the first three, but repeated attempts to induce an antibody response to cotton fibers has been unsuccessful, attempts are still continuing employing higher antigen concentrations.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Anti-Neoplastic Therapy with L-Asparaginase (NSC-109229).

WORK UNIT NO.: 73/144

PRINCIPAL INVESTIGATOR: Nicholas J. DiBella, LTC, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To treat patients with acute lymphoblastic leukemia (ALL), refractory to standard chemotherapy, with L-asparaginase.

TECHNICAL APPROACH

Patients meeting selection criteria outlined were treated with L-Asparaginase as per protocol.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 76: 0.0
FY 77: 0.0

PROGRESS

Five patients have been treated:

(1) B. A. - acute lymphocytic leukemia; complete response, relapsing 3 weeks later.

(2) H. L. - blast crisis of chronic granulocytic leukemia, progression of disease.

(3) R. R. A.L.L. who relapsed after 1 yr on maintenance, treated them with Ara-C and L-asparaginase X3 courses with no response. Treated with total body irradiation with no response.

WORK UNIT NO.: 73/144

PROGRESS - continued

(4) S. B. - A.L.L. who relapsed after initial remission with COAP. Begun on Ara-C, vincristine, prednisone and L-asparaginase on June 77. Received 3 courses with no response. Now undergoing total body irradiation.

(5) R. G. - A.L.L. relapsed after 1 year in remission. Treated with L-asparaginase, vincristine and high dose methotrexate with no response.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Anti-Neoplastic Therapy with CCNU (NSC-79037) /1-2-chloroethyl)-3-cyclohexyl-1-Nitrosourea/.

WORK UNIT NO.: 73/145

PRINCIPAL INVESTIGATOR: Nicholas J. DiBella, LTC, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To treat patients with advanced Hodgkin's disease, bronchogenic carcinoma or brain tumors (primary or metastatic) with CCNU.

TECHNICAL APPROACH

Patients meeting selection criteria outlined were treated with CCNU as per protocol.

Manpower (in professional man years): 0.3/yr

Funding (in thousands) FY 76: 0
FY 77: 0

PROGRESS

Twenty-one patients have completed therapy with CCNU.

(1) C. M. - CNS fibrosarcoma; progression.
(2) C. C. - Astrocytoma; no change.
(3) H. G. - Glioblastoma multiforme; 50% response.
(4) R. L. - Oat cell carcinoma of lung; stable for 6 weeks, then progression.
(5) J. F. - Squamous cell ca of lung; no change.
(6) C. L. - Glioma; less than 50% remission.

WORK UNIT NO.: 73/145

PROGRESS - continued

(7) M. N. - Glioblastoma multiforme; no change.
(8) M. S. - Glioblastoma multiforme; 50% remission
(9) L. S. - Adenocarcinoma; subjective response then progression.
(10) J. H. - Bronchogenic carcinoma; (with hexamethylmelamine) progression.
(11) P. M. - Squamous cell ca of lung; no change for 5 months, then progression.
(12) G. P. - Astrocytoma; complete remission for 26 months then recurrence.
(13) J. H. - Metastatic melanoma; no response.
(14) J. G. - Squamous cell ca; with mitomycin-C and vincristine; no response.
(15) L. F. - Thalamic glioma; 50% response lasted 2 years prior to relapse.
(16) E. E. - Nondifferentiated large cell ca of lung metastatic to brain. Treated with radiotherapy and CCNU.
(17) R. H. - Mixed glioma dx 1976 treated with radiotherapy and CCNU presently stable without evidence of recurrence.
(18) R. Y. - Hodgkin's disease relapsed after radiotherapy and placed on CCNU, velbau, bleomycin, adriamycin, vincristine, and streptozotocin with complete response. Now on maintenance chlorambucil with N.E.D.
(19) W. W. - Grade II astrocytoma treated with radiotherapy and CCNU; 80% restoration of function within 2 months of treatment. Continued on CCNU from 2/74 till 12/76 with no progression. Stable at present.
(20) P. B. - Glioblastoma multiforme; treated with radiotherapy and CCNU with progression.
(21) M. M. - Glioblastoma multiforme; treated with radiotherapy and CCNU with progression.

Publications and Presentations: None

STATUS:

Completed (Drug has become commercially available).

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Use of Daunomycin (NSC-82151) in Acute Leukemia.

WORK UNIT NO.: 73/149

PRINCIPAL INVESTIGATOR: Nicholas J. DiBella, LTC, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To permit use of a drug of proven efficacy in acute leukemia, but which is not yet FDA-approved.

TECHNICAL APPROACH

Patients meeting selection criteria outlined were treated with Daunomycin as per protocol.

Manpower (in professional man years): 0.2/yr

Funding (in thousands) FY 76: 0
FY 77: 0

PROGRESS

(1) T. S. - 28 y/o W/F with AML achieved a complete remission after induction with daunomycin plus Ara-C, 6-TG, vincristine and prednisone. Still in remission.

(2) H. S. - 47 y/o W/F with AML. Expired of intracranial hemorrhage after receiving only one dose of daunomycin.

(3) J. T. - 67 y/o W/M with AML. Treated with daunomycin, Ara-C and 6-TG times one course. Developed a hypocellular marrow, had a CVA and died within 2 months of treatment.

WORK UNIT NO.: 73/149

PROGRESS - continued

(4) B. W. - 50 y/o W/F with AML. Treated with daunomycin, Ara-C, 6-TG, prednisone and vincristine with no response. Died.

(5) M. D. - 50 y/o W/F with AML. Treated with daunomycin, Ara-C, 6-TG and achieved a complete remission. Still in remission.

(6) R. D. - 59 y/o W/M with AML. Treated with daunomycin, Ara-C, 6-TG achieving a complete remission. Still in remission.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Anti-Neoplastic Therapy with BCNU (NSC 409962) / 1,3-BIS (2-chloroethyl)-1-Nitrosourea/.

WORK UNIT NO.: 73/150

PRINCIPAL INVESTIGATOR: Nicholas J. DiBella, LTC, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To treat patients with inoperable or recurrent melanoma, gastrointestinal tumors or brain tumors (primary or metastatic) and refractory multiple myeloma with BCNU.

TECHNICAL APPROACH

Patients meeting selection criteria outlined were treated with BCNU as per protocol.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 76: 0
FY 77: 0

PROGRESS

Thirteen patients were treated.

(1) F. B. - Melanoma - Over 50% remission of 8-9 months' duration.

(2) M. Z. - Hodgkin's disease; no response.

(3) M. E. - Melanoma; progression after 4 months of stable disease.

(4) M. L. - Melanoma; 50% remission.

(5) U. E. - Melanoma; with DTIC and Hydroxyurea; partial response.

WORK UNIT 73/150

PROGRESS - continued

(6) O. J. - Melanoma; with DTIC; no response

(7) J. G. - Adenocarcinoma; progression (with 5FU).

(8) W. F. - Adenocarcinoma of stomach; progression (with 5FU).

(9) T. B. - Lymphoma; given as adjuvant with cytoxan, vincristine and prednisone after surgical resection of recurrence. Now no evidence of disease.

(10) J. J. - Multiple myeloma; relapsed after treatment with alkeran and prednisone and begun on adriamycin and BCNU Jun 76 to Jan 77 with stable disease but now has recurred with progression.

(11) J. O. - Adenocarcinoma head of pancreas; treated with radiotherapy and 5FU plus BCNU; no response.

(12) R. M. - Pancreatic carcinoma; treated with 5FU and BCNU with stable disease for six months then progression.

(13) J. V. - Multiple myeloma; relapsed on alkeran and prednisone and begun on adriamycin and BCNU on June 76. Still on same regimen doing well.

Publications and Presentations: None

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Immuno-chemical Evaluation of Myeloproliferative and Plasmaproliferative Diseases.

WORK UNIT NO.: 74/101

PRINCIPAL INVESTIGATOR: Nicholas J. DiBella, LTC, MC

ASSOCIATE INVESTIGATOR: George L. Brown, LTC, MSC, Ph.D.

OBJECTIVES

To determine whether there are any disturbances of immunoglobulin production or of delayed hypersensitivity in the myeloproliferative diseases. To apply new immunochemical techniques for the characterization of monoclonal gammopathies and other dysproteinemias.

TECHNICAL APPROACH

This is an in-depth immunologic evaluation of patients with myeloproliferative and plasmaproliferative disorders.

Manpower (in professional man years): 0.5/yr

Funding (in thousands) FY 76: 3.0
FY 77: 3.0

PROGRESS

Myeloproliferative Disorders

Five patients have been studied with the following results.

(1) G. B. - Idiopathic thrombocythemia, with depressed serum IgM level and lymphocyte response to PHA.
(2) J. L. - Rule out myeloproliferative disorder; normal T and B cell studies.
(3) E. H. - CML with decreased serum IgM levels, response to PHA, PWM and decreased T cells by rosette studies.
(4) M. D. - CML with depressed responses to PHA and PWM only.

WORK UNIT 74/101

PROGRESS - continued

(5) M. W. - Agnogenic myeloid metoplasia with depressed serum IgG level and no response to PHA and PWM; the number of T cells was also decreased.

Plasmaproliferative Disorders

Seven patients were evaluated.

(1) B. L. - Had an IgM monoclonal gammopathy with a decreased IgG and free kappa chains in the serum.
(2) D. C. - A patient with immunoblastic lymphadenopathy was found to have only a decreased response to PHA.
(3) D. N. - Rule out myeloma; studies were normal.
(4) A. M. - Waldenstrom's macroglobulinemia with marked elevation of serum IgM and hyperviscosity with decreased serum IgG, A and C3; pyroglobulins also found.
(5) E. F. - Waldenstrom's macroglobulenemia with a IgM kappa and decreased IgG and C3.
(6) E. T. - Rule out myeloma; normal studies.
(7) E. O. - Rule out myeloma; free kappa chains found in serum but no other evidence of a monoclonal gammopathy.

Publications:

(1) Brown, G.L., DiBella, N.J., and Corby, D.G.: IgE-IgM Kappa Gammopathy Associated with Lymphocytic Lymphoma. Federation Proceedings 35:438, 1976.

(2) DiBella, N.J., and Brown, G.L.: Immune Dysfunction in the Myeloproliferative Disorders. Manuscript accepted by Cancer.

Presentations:

(1) DiBella, N.J., and Brown, G.L.: Cellular and Humoral Immunity in the Myeloproliferative Disorders. Presented: Annual Joint Meeting of the American College of Physicians and American Society of Internal Medicine, Colorado Regional Meeting, Colorado Springs, Colorado, January 15, 1976.

(2) Brown, G.L., DiBella, N.J., and Corby, D.G.: IgE-IgM Kappa Gammopathy Associated with Lymphocytic Lymphoma. Presented: Federation of American Societies for Experimental Biology, Anaheim, California, April 12, 1976.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Immunologic Effects of Endocrine Manipulation in DMBA-Induced Rat Mammary Neoplasms.

WORK UNIT NO.: 74/106

PRINCIPAL INVESTIGATOR: Nicholas J. DiBella, LTC, MC

ASSOCIATE INVESTIGATOR: George L. Brown, LTC, MSC, Ph.D.

OBJECTIVES

To determine if the therapeutic efficacy of hormonal maneuvers in experimental rat mammary carcinoma is mediated by immunologic mechanisms.

TECHNICAL APPROACH

Serologic and all - mediated immunity was evaluated in rats with DMBA induced mammary tumors before and after combined oophorectomy-adrenalectomy compared with controls who: 1) had the tumors but did not undergo these surgical procedures and 2) controls without tumors who underwent the surgery.

Manpower (in professional man years): 1.0/yr

Funding (in thousands) FY 76: 2.0
FY 77: 0

PROGRESS

The study has been completed. Preliminary analysis of the data indicates that:

1) The surgical procedures failed to alter B-cell function.
2) Oophorectomy and adrenalectomy resulted in a delayed improvement in T-cell function (PHA response) during the 30 to 60 days after surgery particularly when there was a resultant tumor regression.
3) The improvement in T-cell function appeared to accompany rather than precede the tumor response suggesting that this immune phenomenon represented another manifestation of response to the ablative procedure rather than the mechanism for the response.

WORK UNIT 74/106

Publications: Abstract in preparation.

Presentations: None

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Reactive Hypoglycemia: An Analysis of Glucose-Insulin-Glucagon Interrelationships and Counter Hormonal Regulatory Factors.

WORK UNIT NO.: 74/110

PRINCIPAL INVESTIGATOR: Fred D. Hofeldt, LTC, MC

ASSOCIATE INVESTIGATORS: Gary L. Treece, MAJ, MC
M.A. Charles, LTC, MC
T.P. O'Barr, Ph.D., DAC

OBJECTIVES

The objective of the hypoglycemic study is to continue to investigate in our large clinic population the glucose-insulin-glucagon and prolactin interrelationships and the response of counter-regulatory hormones to hypoglycemic stress. This project is a continuation of a previous project initiated in 1969 at the University of California Medical Center, Moffatt Hospital, San Francisco, California.

TECHNICAL APPROACH

The clinical research protocol involves evaluation of control subjects and hypoglycemic patients to assess the interrelationships of beta cell and alpha cell responsiveness to oral and intravenous glucose administration. Based upon findings in controls and patients with disease states, a classification system has been proposed and this experience has been used in determining the basic pathophysiology of reactive hypoglycemic disorders. The clinical studies are being conducted in the Department of Medicine, Endocrine Clinic, with the assistance of an assigned GS-5 to perform blood sampling and assist during the testing. During the glucose tolerance test, the patient has an indwelling catheter for frequent sampling of blood glucose and is continually monitored with a cardiac monitor system and blood glucoses are assessed immediately after sampling by the Ames Reflectance Meter. After glucose administration, blood insulins, glucagons, growth hormones, prolactins and cortisols are sampled and the values are determined by a sensitive radioimmunoassay. The procedure is designed to provide a minimum of patient inconvenience in the performance of these well standardized

WORK UNIT 74/110

TECHNICAL APPROACH - continued

procedures. Many normal individuals experience a low blood sugar state sometime after glucose administration and the clinical significance of a low blood glucose state is observed by recording appropriate adrenergic symptoms at the nadir of the glucose and determining if there is a counter hormonal responsiveness in defending the low blood glucose state as manifested by timely rises in cortisol and growth hormone indicating hypothalamic-pituitary-end-organ stress.

Manpower (in professional man years): 2.0/yr

Funding (in thousands) FY 76: 6.0
FY 77: 8.0

PROGRESS

Approximately 300 oral glucose tolerance tests have been performed since inception of the study. The data derived from these studies have been applied to advancement of the medical understanding of reactive hypoglycemic disorders and for specific patient management. The data has been put on computer tapes by a biostatistician at the University of North Dakota and is retrievable for analysis if these tapes could be adapted to the computers at Fitzsimons Army Medical Center. To continue the project, further funding along the previous guidelines is needed to continue the clinical studies in patients with disordered carbohydrate metabolism. However, additional funds will be needed for the computer expansion of this study for continued input and analysis of the data on this large group of patients. The consultant fees, to include travel, honorarium and quarters for a biostatistician is requested for the continuation of the project. Dr. George Logan, biostatistician at the University of North Dakota has done two years of data compiling on this project and is most suitable to act as consultant to the project for the conversion of the data forms as presently recorded to the Fitzsimons computers. An additional $1000 is requested for this important upgrading of this project which has accumulated such large stores of research data.

Publications:

(1) Hofeldt, F.D., Dippe, S., and Forsham, P.: Diagnosis and Classification of Reactive Hypoglycemia Based on Hormonal Changes in Response to Oral and Intravenous Glucose Administration. Am J Clin Nutrition 25:1193-1202, 1972.

WORK UNIT NO.: 74/110

Publications - continued

(2) Hagler, L., Hofeldt, F.D., Lufkin, E.G., Herman, R.H.: Reactive Hypoglycemia: A Clinical-Physiologic Approach to Diagnosis and Treatment. Rocky Mountain Medical Journal 70:41, 1973.

(3) Anthony, D., Dippe, S., Hofeldt, F.D., Davis, J.W., Forsham, P.H.: Personality Disorder and Reactive Hypoglycemia: A Quantitative Study. Diabetes 22:664, 1973.

(4) Hofeldt, F.D., Lufkin, E.G., Hagler, L., Block, M.B., Dippe, S., Davis, J.W., Levin, S., Forsham, P.H., Herman, R.H.: Are Abnormalities in Insulin Secretion Responsible for Reactive Hypoglycemia. Diabetes 23:589, 1974.

(5) Hofeldt, F.D., Adler, R.A., Herman, R.H.: Postprandial Hypoglycemia: Fact or Fiction. JAMA 233:1309, 1975.

(6) Hofeldt, F.D.: Progress in Endocrinology and Metabolism: Reactive Hypoglycemia. Metabolism 24:1193, 1975.

(7) Hofeldt, F.D., Lufkin, E.G., Hall, S., Dippe, S., Davis, J.W., Levin, S., Forsham, P.H.: Alimentary Reactive Hypoglycemia: Effects of DBI and Dilantin® on Insulin Secretion. Military Medicine 140:841, 1975.

(8) Block, M.B., Hofeldt, F.D., Lufkin, E.G., Hagler, L., Herman, R.H.: The Response of Glucagon-Like Immunoreactivity to Reactive Hypoglycemia. Military Medicine 142:32, 1977.

(9) Hofeldt, F.D.: The Treatment of Reactive Hypoglycemia. Current Therapy, Conn, 452, 1977.

(Published Abstracts):

(1) Block, M.B., Hofeldt, F.D., Lufkin, E., Hagler, L., Herman, R.: Stimulation of Pancreatic Glucagon-Like Immunoreactivity (GLI) by Reactive Hypoglycemia. Diabetes 22:303, 1973.

(2) Hofeldt, F.D., Lufkin, E., Hagler, L., Block, M., et al: Is Delayed Insulin Secretion Responsible for Reactive Hypoglycemia? Diabetes 22:304, 1973.

(3) Hagler, L., Hofeldt, F.D., Lufkin, E., et al: A Clinical Physiological Approach to the Diagnosis and Treatment of Reactive Hypoglycemic Disorders. Colorado Regional Meeting, American College of Physicians, 11-13, January 1973.

WORK UNIT NO.: 74/110

Published Abstracts - continued

(4) Hofeldt, F.D., Dippe, S., Forsham, P.H.: Diagnosis and Classification of Reactive Hypoglycemia Based on Hormonal Changes in Response to Oral and Intravenous Glucose Administration. Excerpta Medico, Endocrinology 28:577, 1973.

(5) Hofeldt, F.D., Lufkin, E.G., Hagler, L., et al: Reactive Hypoglycemia Seen Dependent on Patient Status. Diabetes Outlook 8:9, Nov/Dec 1973.

(6) Block, M.B., Hofeldt, F.D., Lufkin, E.G., et al: Glucagon Response to Hypoglycemia Tied to Symptoms - not Glucose Levels. Diabetes Outlook 9:4, Apr 1974.

(7) Hofeldt, F.D., Lufkin, E.G., Hagler, L., et al: Those with Reactive Hypoglycemia Have Delay on Excess Insulin Response. Internal Medicine News 8:35, 1975.

(8) Hofeldt, F.D., Lufkin, E.G., Hagler, L., et al: Response to Oral Glucose in Reactive Hypoglycemia Often Delayed Or Excessive. Family Practice News 5:64, 1975.

(9) Hofeldt, F.D.: Reactive Hypoglycemia. Diabetes 25:156, 1976.

(10) Hofeldt, F.D., Dippe, S.E., Levin, S.R., et al: Effects of Diphenylhydantoin on Glucose-Induced Insulin Secretion in Three Patients with Insulinoma. Yearbook of Endocrinology 1975, p. 277.

(11) Hofeldt, F.D., Lufkin, E.G., Hagler, L., et al: Are Abnormalities in Insulin Secretion Responsible for Reactive Hypoglycemia. Yearbook of Medicine, 1976, pp. 596-597.

(12) Plymate, S.R., Hofeldt, F.D., Adler, R.A.: Determinants of Glucagon Response in Reactive Hypoglycemia. Clinical Research 25:2, 1977.

Presentations:

(1) Hofeldt, F.D., Sussman, K.: Hypoglycemia. Presented: Department Medicine Grand Rounds, University of Colorado, Denver, Colorado, August 1972.

(2) Hofeldt, F.D.: Is Delayed Insulin Secretion Responsible for Reactive Hypoglycemia? Presented: American Diabetes Association, Chicago, Illinois, June 1973.

(3) Hofeldt, F.D.: New Approaches to the Study of Hypoglycemia. Presented: Regional Meeting for Affiliates of the American Diabetes Association, Grand Forks, North Dakota, December 1974.

WORK UNIT NO.: 74/110

Presentations - continued

(4) Hofeldt, F.D.: The Problems of Hypoglycemia. Presented: Minnesota Academy of Family Physicians, Detroit Lakes, Minnesota, August 1976.

(5) Hofeldt, F.D.: Reactive Hypoglycemia. Presented: 1976 Symposium on Diabetes Mellitus, Mankato, Minnesota, October 1976.

(6) Hofeldt, F.D.: Hypoglycemia - Current Concepts of Diagnosis and Therapy. Presented: Diabetes Symposium, sponsored by The American Diabetes Association of Minnesota, Thief River Falls, Minnesota, March 1977.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Minoxidil as an Antihypertensive in Patients Refractory to Available Medications.

WORK UNIT NO.: 75/102

PRINCIPAL INVESTIGATORS: Harvey A. Gersh, MAJ, MC
Richard G. Pluss, MD, DAC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

The objective of this protocol is to provide an alternative treatment for patients whose blood pressure is refractory to available drugs or who have experienced unacceptable side effects from them. In fulfilling this purpose, the sponsor has been given three important responsibilities by the Food and Drug Administration: (1) Evidence must be provided that the patient(s) in question indeed is refractory to or experiences unacceptable side effects with standard drugs. The Initial Report Form should be completed and submitted to the sponsor *before drug is shipped*; (2) The clinical investigators should be (a) experienced in antihypertensive therapy, (b) familiar with the requirements and precautions associated with new drug testing, and (c) fully informed about the drug on the basis of the protocol supplements and by consultation with the research physician and other minoxidil investigators; and (3) The cases treated must be documented in regard to side effects, safety and the antihypertensive efficacy of the drug in such fashion that the sponsor and, in turn, the FDA are completely and currently involved.

TECHNICAL APPROACH

Stable investigation of the etiology of the hypertension will have been carried out prior to consideration of minoxidil. Assessment of end-organ damage will be part of the record. Behavior of the blood pressure will be documented.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 76: 0.0
FY 77: 0.0

PROGRESS

Since the last progress report, the minoxidil patient population has decreased to nine patients currently under study. One new

WORK UNIT NO.: 75/102

PROGRESS - continued

patient has been added to the study in the last six months. The principal investigator, Dr. John H. Ball, left the Army in 1977. Sufficient clinical data has been accumulated for presentation to clinical meetings. Along these lines, a presentation entitled "The Out Patient Treatment of Refractory Hypertension with Minoxidil" was presented at the Regional American College of Physicians Meeting in Colorado Springs in January 1976. A manuscript entitled "Out Patient Therapy of Refractory Hypertension with Minoxidil" has been submitted for publication. An additional manuscript entitled "Minoxidil-Induced Hypertrichosis: Treatment with Calcium Thioglycolate Depilatory" has been published.

Publications:

(1) Kleiner, J., Ball, J.H., and Nelson, W.A.: The Out Patient Treatment of Refractory Hypertension with Minoxidil. Abstracts. Colorado Regional ACP Meeting Rocky Mountain Medical Journal, p 534, December 1975.

(2) Earhart, R.N., Ball, J.H., Nuss, D.D., and Aeling, J.L.: Minoxidil-Induced Hypertrichosis: Treatment with Calcium Thioglycolate Depilatory. Southern Medical Journal, Vol 70, No 4, April 1977.

Presentations:

(1) Kleiner, J., Ball, J.H., and Nelson, W.A.: The Out Patient Treatment of Refractory Hypertension with Minoxidil. Regional ACP Meeting, Colorado Springs, Colorado, 15-17 January 1976.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: The Incidence of IgG Skin Sensitizing Antibodies in an Allergic Population.

WORK UNIT NO.: 75/103

PRINCIPAL INVESTIGATOR: Harold S. Nelson, COL, MC

ASSOCIATE INVESTIGATOR: L. Bernard Branch, LTC, MC

OBJECTIVES

To determine the incidence of IgG skin sensitizing antibodies among a large group of patients previously skin tested in the Fitzsimons Allergy Clinic.

TECHNICAL APPROACH

The presence of IgG short-term sensitizing antibody in serum previously collected from patients with positive skin tests was monitored employing tests of transfer to macaque monkeys. Differentiation of IgE from IgG skin sensitizing antibody was made by injecting a serum 2, 4, and 24 hours prior to antigen challenge and by heat inactivating some of the serum specimens at 56° for two hours.

Manpower (in professional man years): 0.1/yr

Funding (in thousands)		
	FY 76:	2.0
	FY 77:	1.5

PROGRESS

A total of one hundred sixty-nine passive transfer tests were performed employing one hundred forty-nine different serum specimens, all derived from patients who had 4+ prick tests to the antigen employed in the challenge. In 47% of the passive transfer tests, positive reactions were

WORK UNIT NO.: 75/103

PROGRESS - continued

consistent with an IgE antibody. There were no tests consistent with a short term heat stable antibody as has been described for IgG.

Publications:

(1) Nelson, H.S., Branch, L.B.: Incidence of IgG Short Term Sensitizing Antibodies in an Allergic Population. Accepted for publication, J Allergy Clin Immunol.

Presentations:

(1) Nelson, H.S.: In Search of the IgG Reageen. 5th Annual Meeting Association of Military Allergists, Fitzsimons Army Medical Center, Denver, Colorado, September 23, 1976.

(2) Nelson, H.S.. The Importance of the IgG Short-Term Skin Sensitizing Antibody in Clinical Allergy. 72nd Annual Meeting American Thoracic Society, San Francisco, California, May 16, 1977.

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: The Incidence of Bronchoconstriction Induced by Aspirin, F.D. & C. Dyes, and Food Preservatives in a Group of Severe Perennial Asthmatics.

WORK UNIT NO: 75/105

PRINCIPAL INVESTIGATOR: Harold S. Nelson, COL, MC

ASSOCIATE INVESTIGATOR: Richard Weber, LTC, MC

OBJECTIVES

To determine the incidence of untoward reactions to aspirin, dyes and preservatives in patients with severe and moderately severe bronchial asthma.

TECHNICAL APPROACH

Patients with severe and moderately severe bronchial asthma will be challenged, first openly with aspirin, various food dyes and preservatives in increasing dosages. If these appear to cause attacks of asthma or significant decrease in pulmonary function, challenges will be repeated in double-blind manner.

Manpower (in professional man years): .025/yr

Funding (in thousands)	FY 76:	0
	FY 77:	0

PROGRESS

Forty-one patients have been studied and the results are presently being prepared for publication.

Publications:

(1) Hoffman, M.: Challenges with Aspirin, F.D. & C. Dyes, and Preservatives in Asthma. (Abst.) Journal Allergy & Clinical Immunology, 57:206, 1976.

WORK UNIT NO.: 75/105

Presentations:

(1) Hoffman, M.: Challenges with Aspirin, F.D. & C. Dyes, and Preservatives in Asthma. Presented. 32nd Annual Meeting of the American Academy of Allergy, March, 1976.

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: The Effect of Corticosteroids on Immunoglobulin Levels in Asthmatic Patients.

WORK UNIT NO.: 75/106

PRINCIPAL INVESTIGATOR: William C. Posey, LTC, MC (USAF)

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To determine whether short courses of high-dose corticosteroids administered to asthmatic patients affect their immunoglobulin levels.

TECHNICAL APPROACH

Blood will be collected on patients who receive brief high-dose courses of corticosteroid treatment with follow-up immunoglobulin levels over a period of several weeks after completion of the treatment.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 76: 1.5
FY 77: 0.5

PROGRESS

The immunoglobulin levels were compared in twenty-one patients who received brief high-dose corticosteroid treatment and twenty patients who did not receive corticosteroid therapy.

Publications:

(1) Posey, W.C., Nelson, H.S., Branch, L.B., and Perlman, B.S.: The Effects of Therapeutic Doses of Corticosteroids on Immunoglobulin Levels. Proceedings of the 5th Annual Meeting Association of Military Allergists, p. 32, 1976. Submitted for publication, J Allergy Clin Immunol.

WORK UNIT NO.: 75/106

Presentations:

(1) Posey, W.C.: The Effects of Therapeutic Doses of Corticosteroids On Immunoglobulin Levels. 5th Annual Meeting Association of Military Allergists, Fitzsimons Army Medical Center, Denver, Colorado, September 22, 1976.

(2) Posey, W.C.: The Effect of Corticosteroid on Immunolgobulin Levels The American Congress of Allergy and Immunology, New York, New York, March 31, 1977.

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: A Comparison of the Results of Hyposensitization with Aqueous Grass Extract and Aluminum Precipitated Aqueous Extracted Grass Extract in the Treatment of Patients with Allergic Symptoms Due to Grass Allergy.

WORK UNIT NO.: 75/107

PRINCIPAL INVESTIGATOR: Harold S. Nelson, COL, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To compare the efficacy and side effects of two different types of FDA approved grass extracts.

TECHNICAL APPROACH

Alternate consenting patients requiring grass hyposensitization will receive the aqueous or the alum-precipitated extract. Their charts will be carefully monitored for incidence of local and systemic reactions, number of injections required to reach maintenance therapy. Symptoms during grass pollen exposure, and antibody changes as a result of hyposensitization will be measured.

Manpower (in professional man years): 0.04/yr

Funding (in thousands) FY 76: 1.5
FY 77: 2.5

PROGRESS

No new patients were enrolled during FY 77. Thirty-six patients of the original study group have continued in their third year of observation. The results of the first two years of immunotherapy were analyzed by RAST determination of their specific IgE levels to grass. Thus far the decline in IgE has been comparable for the two groups.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Antineoplastic Therapy with CIS-Platinum (II) Diamminechloride (NSC 119875).

WORK UNIT NO.: 75/110

PRINCIPAL INVESTIGATOR: Nicholas J. DiBella, LTC, MC

ASSOCIATE INVESTIGATOR: John C. Michalak, MAJ, MC

OBJECTIVES

To treat patients with advanced solid tumors, primarily testicular tumors.

TECHNICAL APPROACH

Patients meeting selection criteria outlined were treated with CIS-Platinum as per protocol.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 76: 0.0
FY 77: 0.0

PROGRESS

Three patients have been treated during the past FY:

1) O.H. - 45 -year-old BM with metastatic head and neck carcinoma - no response.

2) B.G. - 38-year-old WM with wide head and neck carcinoma squamous - no response.

3) S.V. - 25-year-old WM with metastatic testicular carcinoma, CIS-platinum used in combination with velban and bleomycin. Complete remission for five months. Primary toxicity has been an transient rise in creatinine and BUN. There has been no irreversible renal toxicity.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: An Evaluation of the Role of Adrenergic Bronchodilators in Patients with Bronchial Asthma on Optimal Doses of Theophylline.

WORK UNIT NO.: 75/112

PRINCIPAL INVESTIGATOR: Harold S. Nelson, COL, MC

ASSOCIATE INVESTIGATOR: L. Bernard Branch, LTC, MC

OBJECTIVES

To determine whether in patients with bronchial asthma who have optimal doses of oral theophylline, the addition of beta adrenergic bronchodilators would produce any significant further improvement of pulmonary function.

TECHNICAL APPROACH

Optimal theophylline dosage will be determined for individual based on theophylline blood levels. The patients response to sympathomimetic bronchodilators in a double-blind and placebo controlled study will then be determined.

Manpower (in professional man years): 0

Funding (in thousands) FY 76: .9
FY 77: 0

PROGRESS

No patients have entered this study which has to a large extent been replaced by protocol 76/110.

Publications and Presentations: None

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Study of the Impaired Water Excretion in Primary Hypothyroidism.

WORK UNIT NO.: 75/113

PRINCIPAL INVESTIGATOR: Fred D. Hofeldt, LTC, MC

ASSOCIATE INVESTIGATORS: Gary L. Treece, MAJ, MC
M.A. Charles, LTC, MC
Paul D. Miller, MD
Robert J. Anderson, MD
Robert W. Schrier, MD
Gary Robertson, MD
Peter Steele, MD
Clifford Zwillich, MD

OBJECTIVES

The study is assessing the role of thyroid hormone in relation to the development of hyponatremia and impaired free water clearance as observed in clinical hypothyroid states.

TECHNICAL APPROACH

Before and after thyroid replacement, hypothyroid patients undergo PAH and insulin clearances, response to a water load and mannitol infusion. Blood and urine are analyzed for osmolality, electrolytes and creatinine. Plasma ADH and prolactin response to these maneuvers are also measured. Cardiac output is measured by Indium ^{131}.

Manpower (in professional man years): 1.0/yr

Funding (in thousands) FY 76: 2.0
FY 77: 2.0

PROGRESS

During the past fiscal year, seven patients with mild hypothyroidism and three patients with moderate to severe hypothyroidism have been studied as outlined above. All procedures have worked well without

WORK UNIT NO. 75/113

PROGRESS - continued

complications. Patients with mild hypothyroidism are able to excrete approximately 2/3 of a water load, whereas the more severely hypothyroid can only excrete about 1/4 of this. Normals and these patients after thyroid hormone replacement excrete 100% of the water load. There seems to be a change in glomerular filtration rate (GFR) causing this. This decreased GFR is not due to decreased cardiac output. Preliminary data suggest no change in ADH or prolactin accounting for the inability to excrete a water load. The data is now being compiled and analyzed and prepared for publication. It is the consensus of the investigators that the paper is most suited for the Journal of Clinical Investigation.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: A Phase I Study of Combination Chemotherapy for Advanced Hodgkin's and Non-Hodgkin's Lymphomas with Adriamycin (NSC 123127), Bleomycin (NSC 125066) and ICRF-159 (NSC 129943).

WORK UNIT NO.: 75/115

PRINCIPAL INVESTIGATOR: Nicholas J. DiBella, LTC, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

1. To determine the efficacy of bleomycin, adriamycin and ICRF-159 in advanced Hodgkin's and non-Hodgkin's lymphomas.

2. To define the schedule and dosage of these drugs which is best tolerated for a subsequent Phase II study.

3. To determine whether ICRF-159 in combination with adriamycin diminished the cumulative cardiotoxicity due to adriamycin.

TECHNICAL APPROACH

A combination of the above agents is to be used in the treatment of advanced lymphomas.

Treatment schedule is as follows:

Drug	Dose	Route	Schedule
Bleomycin	8 mg/M^2	IM	Days 1, 4, 8 and 11
ICRF-159	500 mg/M^2	P.O.	Days 3 and 4
Adriamycin	60 mg/M^2	I.V.*	Day 4 (with ICRF)

*through running I.V.

Rest Period.....Days 12 to 21

ICRD doses will be escalated according to marrow tolerance.

WORK UNIT NO.: 75/115

TECHNICAL APPROACH - continued

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 76: 0
FY 77: 0

PROGRESS

No further patients have been placed on this study due to the closure of The Western Cancer Study Group. The Principal Investigator does not feel the study is worth pursuing without having this access to a large number of patients.

Publications and Presentations: None

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Fractionation of Kochia (Kochia Scoparia) Pollen with Isolation of Kochia Pollen Extract Antigens.

WORK UNIT NO.: 75/116

PRINCIPAL INVESTIGATOR: Mark R. Stein, MAJ, MC

ASSOCIATE INVESTIGATORS: Harold S. Nelson, COL, MC
Thomas P. O'Barr, Ph.D., DAC

OBJECTIVES

This study is designed to extract raw kochia pollen and purify it through chemical fractionation. It will attempt to isolate antigenic molecules of significance in human allergy (to this plant).

TECHNICAL APPROACH

Raw kochia defatted pollen has been extracted in distilled water and aliquots separated. This material has been used to immunize rabbits emulsified in Freund's complete adjuvant, and rabbit antisera have been obtained. Allergic human sera are currently available at -70°C. Kochia discs will be used in the direct RAST to determine which human sera will be pooled and in the indirect RAST to determine antigenic activity of isolated kochia fractions. Macaque monkeys will also be used by pca to test the extract potency.

Manpower (in professional man years): 0.1/yr

Funding (in thousands)		
	FY 76:	1.5
	FY 77:	2.5

PROGRESS

Initial attempts at fractionation of Kochia revealed no evidence of RAST inhibiting activity in association with the protein peaks. Several modifications in the technical procedure of fractionation by Dr. O'Barr have resulted in fractions which react with rabbit antisera raised against the Kochia extract and these specimens are now awaiting RAST analysis for relevant allergenicity.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Evaluation of Inhaled Cromolyn Sodium in the Treatment of Seasonal Asthma.

WORK UNIT NO.: 75/117

PRINCIPAL INVESTIGATOR: Dudley A. Raine, Jr., LTC, MC

ASSOCIATE INVESTIGATORS: L. Bernard Branch, LTC, MC
Harold S. Nelson, COL, MC

OBJECTIVES

To determine the efficacy of inhaled sodium cromolyn in the treatment of seasonal allergic bronchial asthma.

TECHNICAL APPROACH

Suitable patients from the Allergy Clinic at Fitzsimons Army Medical Center with fall seasonal asthma or perennial asthma with fall exacerbations are screened for selected criteria. If they are interested in participating in the study, written informed consent is obtained and initial history and physical examination is obtained. Appropriate skin testing for weed sensitivity is done if recent skin test results are not in their records. Baseline pulmonary function tests, chest x-ray, CBC, UA and 12 chemistries are obtained. The patient is then given a supply of medication which is double blinded, a spin haler for administration, a daily record sheet, a Wright Peak Flow Meter and written instructions as well as on oral review on how to participate in the study. At the onset of the symptoms of asthma for that fall season, the patient will begin the study, carefully recording daily his symptoms, the amount of medication he is using and twice daily peak flow readings. They will be followed by a clinic visit every two weeks with a history, physical exam and pulmonary functions. Blood will be obtained at the beginning and the end of study, and analyzed by RAST for levels of specific IgE antibodies directed toward ragweed, Russian thistle and sage.

WORK UNIT NO.: 75/117

TECHNICAL APPROACH - continued

Manpower (in professional man years): 0.05/yr

Funding (in thousands) FY 76: 1.0
FY 77: 1.0

PROGRESS

No further patients were enrolled in this study due to the departure of Drs. Raine and Branch and the difficulty in finding appropriate individuals with clear allergic asthma in this locality.

Publications and Presentations: None

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: A Study of the Stability of Allergy Extracts Under Varying Conditions.

WORK UNIT NO.: 75/118

PRINCIPAL INVESTIGATOR: Harold S. Nelson, COL, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To systematically explore the effects of several stabilizers on the loss of potency of allergy extracts at different concentrations, volumes and time intervals.

TECHNICAL APPROACH

Varying dilutions of Russian thistle allergy extract will be prepared from identical freeze-dried lots. These will be stabilized with varying concentrations of human-serum albumin or tween or glycerine or no stabilizaing agent. They will be placed in both siliconized and plain vials. New dilutions will be set up periodically during the course of a year and at the end of one year's time, the continuing potency of the extracts will be compared using skin testing in human volunteers and RAST inhibition curves.

Manpower (in professional man years): 0.04/yr

Funding (in thousands) FY 76: 0
FY 77: 4.0

PROGRESS

The extracts were analyzed in May and June 1977 for residual activity as compared with fresh dilutions from the same freeze-dried extract. Testing was done by RAST inhibition. The results of the study are currently being analyzed.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Fluoridated Tooth Paste as the Possible Agent Responsible for Perioral Dermatitis.

WORK UNIT NO.: 75/119

PRINCIPAL INVESTIGATOR: J. Ramsey Mellette, Jr., MAJ, MC

ASSOCIATE INVESTIGATORS: John L. Aeling, COL, MC
Donald D. Nuss, COL, MC

OBJECTIVES

To determine if fluoridated tooth paste causes or greatly enhances the development of perioral dermatitis.

TECHNICAL APPROACH

Patients have been entered into a randomized double-blind cross-over study with tooth pastes that are identical except that one contains 0.5% stannous fluoride. The patients are to be crossed over after two months use of the tooth paste if no dermatitis develops. If a significant perioral dermatitis develops, they may be crossed over earlier.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 76: 0
FY 77: 0

PROGRESS

A total of sixteen patients were entered into the study. Four patients developed a flare of their perioral dermatitis on fluoride tooth paste, and one patient worsened on the placebo tooth paste. Major Mellette is no longer assigned to Fitzsimons Army Medical Center and it is felt that the shelf life of the fluoride tooth paste has expired. Major Mellette has all the data from the study and is in the process of writing an article for publication.

WORK UNIT NO.: 75/119

Publications:

(1) Mellette, J.R., Aeling, J.L., and Nuss, D.D.: Fluoride Tooth Paste: A Cause of Perioral Dermatitis. Arch of Derm, Vol. 112, No. 5, 1976.

Presentations: None

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Study of ICRF-159 (NSC 129943) Given Orally Plus Radiation Therapy for the Treatment of Bronchogenic Carcinoma.

WORK UNIT NO.: 75/120

PRINCIPAL INVESTIGATOR: Nicholas J. DiBella, LTC, MC

ASSOCIATE INVESTIGATOR: Kenneth D. Herbst, MAJ, MC

OBJECTIVES

To assess the toxicity and tolerance to a regimen of ICRF-159 combined with conventional radiation therapy in patients with unresectable non-oat cell bronchogenic carcinoma.

TECHNICAL APPROACH

Patients who met criteria for selection and who agreed to participate in the study were treated with ICRF-159 in combination with radiation therapy as outlined in the protocol.

Manpower (in professional man years): 0.1/yr

Funding (in thousands)		
	FY 76:	0
	FY 77:	0

PROGRESS

One additional patient (WR) has been entered in the study and has remained on maintenance therapy for 10 months free of recurrence of tumor and without significant toxicity. No further patients will be entered and the protocol will be terminated because of inadequate patient accrual.

Publications and Presentations: None

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: The Blocking Effect of SCH 1000 and/or Isoproterenol upon the Bronchoconstrictive Action of Antigen Inhalation Challenge.

WORK UNIT NO.: 75/122

PRINCIPAL INVESTIGATORS: Mark R. Stein, MAJ, MC
Sheldon L. Spector, M.D.

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

This study is designed to determine the blocking effect on antigen induced bronchospasm of: SCH 1000, an atropine-like medication, isoproterenol and the combination of SCH 1000 and isoproterenol. It is also designed to evaluate the systemic effects, if any, and side effects of these blocking agents.

TECHNICAL APPROACH

At Fitzsimons Army Medical Center, Allergy Clinic, suitable patients with reagin mediated asthma are screened for selection criteria. If they are interested in participating in this study, informed consent is obtained to perform a history and physical exam and an isoproterenol inhalation test. Patients who are acceptable by study criteria are then referred to National Jewish Hospital, Denver, Colorado. There they must meet criteria of stability of asthma and a positive antigen bronchial challenge, before they are eligible to enter the double-blind study using placebo, SCH 1000, isoproterenol, or the combination of SCH 1000 and Isoproterenol.

Manpower (in professional man years): 0

Funding (in thousands) FY 76: 0
FY 77: 0

PROGRESS

This study was terminated by the manufacturer due to the discovery of instability of the SCH 1000. The drug is currently being withdrawn from investigative studies.

Publications and Presentations: None

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: A Long-Term Efficacy and Safety Study of Albuterol Tablets and Syrup in Children 6-14 Years Old.

WORK UNIT NO.: 75/123

PRINCIPAL INVESTIGATOR: Harold S. Nelson, COL, MC

ASSOCIATE INVESTIGATOR: W.C. Doner, LTC, MC

OBJECTIVES

(1) To determine the efficacy, safety, and tolerance of albuterol tablets and syrup when administered for periods of up to 12 months in children 6-14 years of age.

(2) To determine the spectrum and frequency of side effects which may be associated with chronic treatment with albuterol tablets or syrup.

(3) To determine the potential for diminished therapeutic response when albuterol tablets or syrup are administered regularly for periods of up to 12 months.

TECHNICAL APPROACH

Patients will be placed on a dose of albuterol, either four milligrams q.i.d. or six milligrams q.i.d., guided by their demonstrated tolerance for these dosages in the previous study. Patients will keep a twice daily symptom diary and record twice daily peak flows for the first two months of the study. Thereafter, they will not record symptoms or pulmonary function.

Patients will have their response to albuterol measured at three-month intervals, at which time they will report to the Allergy Clinic at 8:00 o'clock for at least six hours prior to the visit. After baseline pulmonary function, pulse and blood pressure measurements have been obtained, they will receive either four or six milligrams of albuterol and their response will be monitored for the succeeding six hours.

Manpower (in professional man years): .05/yr

Funding (in thousands)	FY 76:	0
	FY 77:	0

WORK UNIT NO.: 75/123

PROGRESS

A six-month study of nineteen children was completed.

Publications:

(1) Nelson, H.S., Raine, D., Doner, H.C., Posey, W.C.: Sub-Sensitivity to the Bronchodilator Action of Albuterol Produced by Chronic Administration. Accepted for publication, Am Rev Res Dis. (Nov 1977)

Presentations: None

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: A New Measure of Anatomic Dead Space During Steady State Studies: Theory - Component Design.

WORK UNIT NO.: 76/100

PRINCIPAL INVESTIGATOR: David R. Hazlett, COL, MC

ASSOCIATE INVESTIGATOR: Neal B. Kindig, Ph.D.

OBJECTIVES

To develop a method to measure anatomic dead space during steady state diffusing capacity studies. To develop a valve to be used in the measure of anatomic dead space during steady state diffusing capacity studies.

TECHNICAL APPROACH

A theory of the experiment will be developed using digital computer analysis and simulation on a lung model that consists of a single alveolar compartment in which perfect mixing occurs. The "actual" and "predicted" dead space will be compared. Significant sources of error and fundamental limitations of the method will be identified. Three steps are anticipated in the experimental valve design problem. First, an existing solenoid valve system that was designed for single breath helium measurement will be tried. Second, a commercial valve will be sought with the required control capabilities and capacity. Third, simultaneously with the search for a commercial valve, a study will be made of the flow capacity, port capability and switching speed required for a programmable pulmonary function valve. Several preliminary approaches to valve design including programmable flop and programmable rotary head will be considered. Design specifications for a valve will be proposed.

Manpower (in professional man years): 1/yr

Funding (in thousands)		
	FY 76:	5.0
	FY 77:	5.0

PROGRESS

The theoretical two breath experiment was simulated by digital computer. This proved the correctness of the basic concept,

WORK UNIT NO.: 76/100

PROGRESS - continued

identified potential sources of error and limitations. The error in the estimate was found to increase with increasing tidal volume and with inequality of the tidal volumes of the successive breaths. The error was found to vary with the square of the alveolar dilution ratio $[(Vt - Vd)/(Va + Vt)]^2$ remaining relatively small for ratios up to about 30%. Preliminary theoretical work has been started on an approach to the dead space estimate when successive tidal volumes are unequal. A limited number of experiments have been carried out on the programmed solenoid valve system. The results were encouraging but there are many limitations in this system. Regular breathing is difficult because of the noise and resistance of the valves. Pressure waves created by opening and closing of the valves probably cause errors in the flow and volume measurements. Electrical delay and noise produce erratic timing of the opening and closing of the valves. A valve has been designed for preliminary testing which was found to be encouraging, we plan to "borrow" the University of Colorado's Mass Spectrometer to complete the study.

Publications:

(1) Kindig, N.B., Hazlett, D.R.: A New Measurement of Anatomic Dead Space During Steady State Studies: Theory. *Medical Instrumentation*, 10:69, 1976.

(2) Kindig, N.B., Hazlett, D.R.: Measurement of Anatomic Dead Space During Steady State Studies of Pulmonary Diffusing Capacity. Biomedical Sciences Instrumentation, 12:89-92, 1976.

(3) Kindig, N.B., Hazlett, D.R.: Dead Space Measurement in Lungs with Unequal Distribution of Volumes: Theory. The Physiologist, 19:253, 1976.

(4) Kindig, N.B., Hazlett, D.R.: Anatomic Dead Space - A Multi-breath Measurement Method. Fed. Proc., 36:613, 1977.

Presentations:

(1) Kindig, N.B., Hazlett, D.R.: A New Measurement of Anatomic Dead Space During Steady State Studies: Theory. Presented to the 11th Annual Meeting of the Association for the Advancement of Medical Instrumentation, 22-25 March 1976, Atlanta, Georgia.

WORK UNIT NO.: 76/100

Presentations - continued

(2) Kindig, N.B., Hazlett, D.R.: Measurement of Anatomic Dead Space During Steady State Studies of Pulmonary Diffusing Capacity. Presented to the 13th Annual Rocky Mountain Bioengineering Symposium, 3-5 May 1976, Laramie, Wyoming.

(3) Kindig, N.B., Hazlett, D.R.: Dead Space Measurement in Lungs with Unequal Distribution of Volumes: Theory. Presented to the 27th Annual American Physiological Society Meeting, 15-20 August 1976, Philadelphia, Pennsylvania.

(4) Kindig, N.B., Hazlett, D.R.: Anatomic Dead Space - A Multibreath Measurement Method. Presented to the 61st Annual Meeting of the Federation of American Societies for Experimental Biology, 1-8 August 1977, Chicago, Illinois.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Trial of Lithium Carbonate to Prevent or Reduce Neutropenia in Dogs Receiving Radiation.

WORK UNIT NO.: 76/101

PRINCIPAL INVESTIGATOR: Nicholas J. DiBella, LTC, MC

ASSOCIATE INVESTIGATORS: Donald G. Corby, COL, MC
W. Nicholas Glab, SP6, B.S.

OBJECTIVES

To determine the efficacy of lithium carbonate in preventing or reducing the neutropenia due to myelotoxic irradiation.

TECHNICAL APPROACH

Dogs will be maintained at lithium levels of 1.2-1.5 mEq/l for 21 days, after which half will receive 250 rads of whole body radiation. Bone marrow biopsy, complete blood count with differential, and serum colony stimulating factor will be monitored during the course of the study and compared with control animals.

Manpower (in professional man years): 0.2/yr

Funding (in thousands) FY 76:
FY 77:

PROGRESS

Since inception of the study two problems have been manifested. First, reliable facilities for measuring blood lithium levels have been unavailable. An atomic absorption spectrophotometer has been procured and is being installed, which will alleviate this problem. Secondly, the original protocol utilized rats, which proved in preliminary studies to be an unsuitable animal model due to their high percentage of lymphocytes. The protocol has been rewritten to study lithium carbonate's action in dogs, wherein blood values approach those of humans.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT REPORT
30 SEP 77

TITLE: Anti-neoplastic Therapy with Methyl CCNU (NSC95441)/1-(2-Chloroethyl)-3-(4-Methyl Cyclohexyl)-1-Nitrosourea.

WORK UNIT NO.: 76/102

PRINCIPAL INVESTIGATOR: Nicholas J. D'Bella, LTC, MC

ASSOCIATE INVESTIGATOR: Kenneth D. Herbst, MAJ, MC

OBJECTIVES

To treat patients with inoperable, recurrent or disseminated colorectal carcinoma with MeCCNU.

TECHNICAL APPROACH

Patients meeting selection criteria outlined were treated with MeCCNU as per protocol.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 77: 0

PROGRESS

(1) B.J. - mucoepidemioid carcinoma of appendix; treated with 5Fu + MeCCNU for 3 courses with no response

(2) L.M. - adenocarcinoma colon metastatic to liver; treated with 5Fu + MeCCNU; >50% objective response for 4-5 months, then progression.

(3) L.E. - adenocarcinoma colon metastatic to liver; treated with 5Fu + MeCCNU; >20% <50% response for 6 months, then progression.

(4) P.G. - adenocarcinoma colon metastatic to liver; treated with 5Fu, MeCCNU and mitomycin-C; no response.

(5) W.W. - adenocarcinoma of colon with liver metastasis; treated with 5Fu + MeCCNU from 2/76 till progression on 4/76.

(6) P.B. - adenocarcinoma of colon with pleural involvement. Treated with 5Fu + MeCCNU from December 75 till June 76 at which time patient had no evidence of disease. Presently has no evidence of disease.

WORK UNIT NO.: 76/102

PROGRESS - continued

(7) H.O. - adenocarcinoma of colon metastatic to liver; treated with 5Fu + MeCCNU with no response.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: An Objective Measure of CNS Development in Children.

WORK UNIT NO.: 76/103

PRINCIPAL INVESTIGATORS: R. John Morgan, Ph.D. (CSU, CO)
John H. Buscemi, MAJ, MC

ASSOCIATE INVESTIGATORS: John W. Steadman, Ph.D. (CSU, CO)
C. Norman Rhodine, Ph.D. (CSU, CO)
Paul W. Daugherty, B.S. (CSU, CO)
James W. Howell, B.S. (CSU, CO)

OBJECTIVES

A long-term goal of the proposed research is to develop a clinical method of assessing central nervous system (CNS) development in children too young to be tested using behavioral methods. Early diagnosis of abnormal CNS development is of paramount importance in early institution of therapy which influences the prognosis. Such early diagnosis is not possible using testing methods which require verbal or written communication skills.

TECHNICAL APPROACH

The proposed research will develop a quantitative method of assessing CNS development and the data base for normal subjects. Abnormal development of the CNS, such as mental retardation, will be the subject of a later research. This study is designed to find parameters of the Electroencephalogram (EEG) which will be reliable quantitative measures of CNS development and establish the normal range of these parameters. The variation of these parameters with age in normal children will be established and statistically tested for significance.

Manpower (in professional man years): 0.5/yr

Funding (in thousands) FY 77: 0

PROGRESS

Seventy-three patients have been investigated. Data evaluation has not been completed at this time. A total of 250 patients will be investigated prior to conclusive data evaluation.

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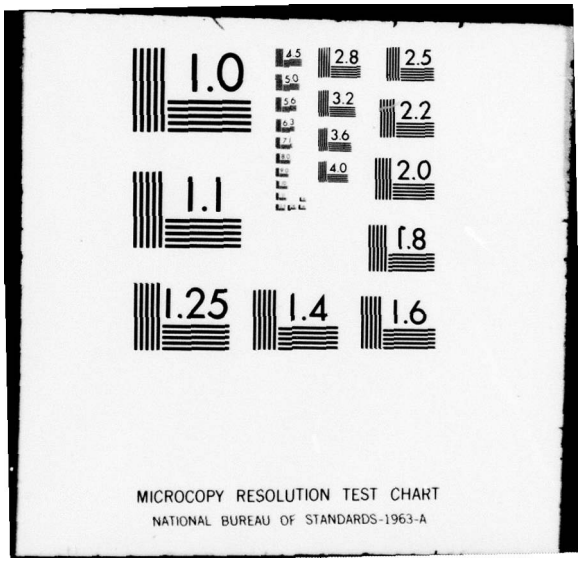
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WORK UNIT NO.: 76/103

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Clinical Trial of Lithium Carbonate to Prevent or Reverse Neutropenia.

WORK UNIT NO.: 76/104

PRINCIPAL INVESTIGATOR: Nicholas J. DiBella, LTC, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To determine the efficacy of lithium carbonate in preventing or reversing neutropenia induced by chemotherapy or reversing chronic neutropenic states.

TECHNICAL APPROACH

Lithium carbonate will be given to patients with chronic neutropenia, after a minimum of 3 weeks baseline observation, to determine whether it can raise the total granulocyte count. It will also be given to patients receiving cyclic chemotherapy to determine if it can diminish the fall (nadir) in granulocyte level following the chemotherapy.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 76: 0
FY 77: 0

PROGRESS

Six patients have been treated with lithium in an attempt to stimulate granulocytosis in patients with chronic neutropenia or to prevent neutropenia in conjunction with chemotherapy. Two patients with bone marrow failure were treated with the lithium without response. One patient (Cook) had hypoplasia of the marrow secondary to prolonged chlorambucil therapy and poorly differentiated lymphocytic

WORK UNIT 76/104

PROGRESS - continued

lymphoma which was in remission at the time. The other patient (Hegy) had a pancytopenia secondary to a hypoplastic marrow which was interpreted as preleukemic in nature. Both patients failed to respond to the lithium and experienced no significant side effects. A third patient (Rimmel) with hairy-cell leukemia also failed to respond to lithium administered over a four week period. A patient with myeloma being treated with Adriamycin and BCNU on a cyclic basis (Vigil) failed to experience an increase in granulocyte count after a brief period of lithium treatment. Due to GI toxicity he could not continue with the lithium beyond four or five days. Another patient (Sather) with lymphosarcoma cell leukemia in remission failed to obtain an increase in granulocyte count while on the lithium compared to previous cycles of chemotherapy without lithium. Only one patient (Silva), receiving cyclic cyclophosphamide, vincristine and prednisone for poorly differentiated lymphocytic lymphoma obtained significant improvement in the granulocyte count during cycles when he was receiving the lithium. The nadir of his granulocyte count after the cycle without lithium was 1,000 compared with a nadir of 2,500 granulocytes while taking the lithium. He experienced no toxicity from the lithium. Aside from GI toxicity in one and mild tremor in another patient there have been no significant side effects from the lithium carbonate.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Evaluation of Testicular Function in Patients Receiving Cytotoxic Therapy.

WORK UNIT NO.: 76/105

PRINCIPAL INVESTIGATOR: Gary L. Treece, MAJ, MC

ASSOCIATE INVESTIGATOR: Nicholas J. DiBella, LTC, MC

OBJECTIVES

To determine if there are abnormalities in testicular function resulting from cytotoxic therapy. To determine whether correction of such hormone deficiencies is beneficial to the patients, particularly by improving their bone marrow function or other testosterone related parameters such as muscle strength, weight gain, etc.

TECHNICAL APPROACH

The patient population under study is that of male patients over the age of 18 years with proven malignancy who are undergoing chemotherapy. To be included in the study the patients must have an expected survival of at least three months, sign a Volunteer Agreement form and be receiving any single cytotoxic agent or combination of such agents. Patients who have received pelvic irradiation or who have undergone bilateral orchidectomy or who have had known diseases of the testes prior to the institution of therapy will be excluded from the study.

Prior to therapy each patient will have a LH, FSH, testosterone and estradiol drawn and a semen analysis obtained. Sexual history will also be monitored in the form of a questionnaire. Patients with decreased testosterone or increased LH will be treated with 200 mg of testosterone enanthate IM every two weeks. All patients will continue to have endocrine studies drawn and questionnaires filled out during their chemotherapy.

Manpower (in professional man years): 0.0/yr

Funding (in thousands) FY 77: 0.0

WORK UNIT NO.: 76/105

PROGRESS

Due to the resignation of the principal investigator no progress has been made on this protocol during the last year. However, the present investigator and associate investigator feel that this protocol indeed has merit and should yield useful information beneficial to the patient population in question and the medical profession alike.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: A Long Term Comparative Efficacy and Safety Study of Albuterol vs. Isoproterenol Nebulizer Solution in the Treatment of Reversible Airway Disease in Adults.

WORK UNIT NO.: 76/106

PRINCIPAL INVESTIGATOR: Harry S. Spaulding, Jr., COL, MC

ASSOCIATE INVESTIGATOR: John T. McDonnell, MAJ, MC

OBJECTIVES

(1) To determine the efficacy, safety, and tolerance of albuterol nebulizer solution when administered by mechanical nebulization for periods of up to six months in patients with reversible airway disease. Clinical efficacy and safety, as well as electrocardiographic indices will be monitored.

(2) To determine the spectrum and frequency of side-effects which may be associated with chronic treatment with albuterol nebulizer solution delivered by mechanical nebulization.

(3) To determine whether the magnitude and duration of bronchodilation is maintained when albuterol nebulizer solution delivered by mechanical nebulizer is used regularly for periods up to six months.

(4) To compare the effects of albuterol with those of isoproterenol nebulizer solution.

TECHNICAL APPROACH

At the present time, this study is approximately 80% complete. We have one more month of investigation to include the full laboratory data during the month of October. To date there have been no major problems, two patients were dropped for failure to comply with the protocol, one patient due to an incidental myocardial infarction not related to the study.

Manpower (in professional man years): 0.5/yr

Funding (in thousands) FY 77:

WORK UNIT NO.: 76/106

PROGRESS

This study has been in progress for the past four months, it is a double-blind study utilizing nebulized or aerosolized bronchodilators either isoproterenol or albuterol. At the present time these chronic asthmatics are still requiring their daily bronchodilators and it is impossible to state whether or not there has been any change in overall management of this chronic condition. No unusual side reactions or abnormalities in x-rays or routine laboratory data have been observed to date. All patients are tolerating the medications as prescribed and the data is merely being collected. At the time the code is broken a statistical analysis is applied, further progress and a realization of pharmacological properties and utilization of albuterol can then be addressed. It was recently discovered that high doses of albuterol have had an adverse effect on mice, therefore, this study will be terminated.

Publications and Presentations: None

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Evaluation for Aspiration in Asthmatics with Gastroesophageal Reflux by Isotope Technique.

WORK UNIT NO.: 76/107

PRINCIPAL INVESTIGATOR: Mark R. Stein, LTC, MC

ASSOCIATE INVESTIGATOR: Nassar Ghaed, LTC, MC

OBJECTIVES

To demonstrate whether broncho pulmonary aspiration occurs in asthmatics with significant gastroesophageal reflux.

TECHNICAL APPROACH

Patients with asthma and evidence of gastroesophageal reflux will be a candidate for study in the hospital in a fasting state. Isotope labelled sulfur colloid will be placed in their stomach at bedtime through a nasal gastric tube. The next morning they will report to the isotope clinic where the lungs will be scanned for evidence of aspiration of the isotope.

Manpower (in professional man years): 0.02/yr

Funding (in thousands) FY 77: 0.5

PROGRESS

Approximately ten patients were studied one or more times, and all studies were negative. The protocol has now been terminated due to the transfer of Dr. Stein to Walter Reed. The data is scheduled for presentation at the upcoming Association of Military Allergists Meeting and will be submitted for publication in the Journal of Nuclear Medicine.

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Correlation of Serum Theophylline Levels in Lower Esophageal Sphincter Pressure.

WORK UNIT NO. 76/108

PRINCIPAL INVESTIGATOR: Mark R. Stein, LTC, MC

ASSOCIATE INVESTIGATOR: Thomas G. Towner, MAJ, MC
Richard Weber, LTC, MC

OBJECTIVES

To demonstrate the degree of correlation between the serum level of theophylline and the lower esophageal sphincter pressure.

TECHNICAL APPROACH

Individuals with and without the symptoms of gastroesophageal reflux will be studied by esophageal manometry before and following the administration of theophylline at a dose calculated to achieve therapeutic blood levels.

Manpower (in professional man years): 0.02/yr

Funding (in thousands) FY 77: 0.5

PROGRESS

Six patients with esophageal reflux and five individuals without esophageal reflux have been studied. The manometry data are available, serum thophyllines will be performed in the near future. The results are scheduled for presentation at the pulmonary symposium in September 1977.

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: An Evaluation of Nasal Secretory IgE.

WORK UNIT NO.: 76/109

PRINCIPAL INVESTIGATOR: John McDonnell, MAJ, MC

ASSOCIATE INVESTIGATOR: Harold S. Nelson, COL, MC

OBJECTIVES

To determine whether a localized secretory IgE response can occur to selected aero allergens in the absence of cutaneous mass cell sensitization and to determine whether this is associated with nasal mass cell sensitivity to these antigens.

TECHNICAL APPROACH

Patients who present to the allergy clinic with a seasonal history of allergic rhinitis but with negative tests to the suggested aero allergens will be the principal subjects for investigation, in addition there will be positive and negative control groups. All groups will be studied by skin testing, serum RAST for the suspected aero allergens, nasal RAST for the suspected aero allergens and nasal antigen challenge.

Manpower (in professional man years): 0.04/yr

Funding (in thousands) FY 77: 0.8

PROGRESS

Approximately ten persons in each of the three groups have now been studied. As soon as RAST materials are available the laboratory work will be performed. Depending upon the results this may constitute completion of the study or modifications of the procedure may be made and further patients studied next year.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: A Study of Terbutaline and Aerosol in the Treatment of Patients with Bronchial Asthma.

WORK UNIT NO.: 76/110

PRINCIPAL INVESTIGATOR: Harold S. Nelson, COL, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To determine the effectiveness of the regular administration of aerosolized terbutaline on patients with mild and moderate bronchial asthma.

TECHNICAL APPROACH

The initial step in this study was the determination of dose response curve to the terbutaline delivered by metered dose inhaler and nebulized by pressure driven nebulizer and IPPP machine. Further studies involve monitoring the response of patients to aerosolized terbutaline during continuous use over a twelve week period. A third portion will be to compare the control of bronchial asthma with optimal doses theophylline or with aerosolized terbutaline.

Manpower (in professional man years): 0.02/yr

Funding (in thousands) FY 77: 0

PROGRESS

The initial dose reponse studies have been performed. The second and third portion of the study are scheduled to begin in approximately two months.

Publications:

(1) Weber, R.W., Nelson, H.S., Petty, W.E.: Dose Response to Aerosolized Terbutaline in Asthmatics: Comparison of Vehicle of Administration. (Abstract) The Am Rev Respiratory Dis, vol 115, part 2, no. 2, p. 78, April 1977.

WORK UNIT NO.: 76/110

Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Study of the Effect of Ibuprofen (Motrin) on Platelets in Normal Subjects.

WORK UNIT NO.: 76/111

PRINCIPAL INVESTIGATOR: John C. Michalak, MAJ, MC

ASSOCIATE INVESTIGATORS: Robert Claypool, MAJ, MC
Judy Barber, GS-9, DAC
Pat Rush, GS-9, DAC

OBJECTIVES

To determine the effect of Ibuprofen on the platelets of a control group of patients who do not have inflammatory joint disease and who are on no other medications.

TECHNICAL APPROACH

Baseline coagulation studies including bleeding time, protime, partial thromboplastin time, platelet count, platelet adhesivity, platelet aggregation with epinephrine, thrombin, collagen, ADP and ristocetin were obtained on 20 normal subjects following informed consent. Repeat studies were done at 24 hrs, 7 days and 8 days to determine if and how long Motrin (Ibuprofen) affected platelet function.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 77: 0.0

PROGRESS

Over the past year 20 normal controls were placed on the Motrin study as described above. It was felt that the study was inadequate due to difficulties with the aggregometer in the coagulation lab, and to poor patient compliance, primarily the ingestion of antihistamines and/or alcohol which affected baseline studies of platelet aggregation. These problems have been presently worked out and it is anticipated that the study will resume January 1978.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Study of the Effect of Tetracycline and Pleural Drainage on Pleural Effusion in Cancer Patients.

WORK UNIT NO.: 76/112

PRINCIPAL INVESTIGATOR: John C. Michalak, MAJ, MC

ASSOCIATE INVESTIGATOR: Michael Barry, LTC, MC
Rex Parker, MAJ, MC

OBJECTIVES

To determine in a prospective, randomized, double-blind fashion if pleural drainage and tetracycline are better than pleural drainage alone in the treatment of pleural effusion in cancer patients.

TECHNICAL APPROACH

Patients with biopsy-proven malignancy with malignant infusion are being randomized to closed chest tube drainage alone or closed chest tube drainage in tetracycline. This is being done in a double-blind manner by the Pharmacy Service so ward physicians do not know if the patient is given tetracycline or the vitamin solution which looks the same as tetracycline.

Manpower (in professional man years): 0.0

Funding (in thousands) FY 77: 0.0

PROGRESS

Patient accrual has been slow and only five patients have presently been entered on the study. The code has not yet been broken so as yet it is uncertain which patients have been treated with closed chest tube drainage alone or closed chest tube drainage in tetracycline. To improve patient accural it is felt that further staffing from the Pulmonary Service is required and this will be done during the next 30-60 days.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Laboratory Evidence of Immune Complexes on Maintenance Immunotherapy for Allergic Rhinitis.

WORK UNIT NO.: 76/113

PRINCIPAL INVESTIGATOR: Mark R. Stein, LTC, MC

ASSOCIATE INVESTIGATOR: Harold S. Nelson, COL, MC
George L. Brown, LTC, MSC

OBJECTIVES

To demonstrate whether patients with allergic rhinitis on immunotherapy are at increased risk of developing circulating immune complexes and possible immune complex disease.

TECHNICAL APPROACH

Patients with allergic rhinitis on maintenance immunotherapy were studied for evidence of circulating immune complexes. The principal techniques employed were cryoglobulins and C1q deviation tests.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 77: 2.0

PROGRESS

A total of fifty patients with allergic rhinitis on maintenance immunotherapy were studied. They were compared with twenty-five patients with allergic rhinitis not on immunotherapy and twenty-five patients with no allergic disease or recent infections. In addition, for the C1q deviation test, forty sera were drawn from patients with seasonal allergic rhinitis who had never received immunotherapy and these were clotted at 37°C in a manner similiar to that for collecting the cryoglobulins. Study of patients is completed, all laboratory results have been completed except the C1q deviation test, results of which are anticipated shortly. As soon as these are obtained a final publication will be submitted.

WORK UNIT NO.: 76/113

Publications: None

Presentations:

(1) Stein, M.R.: Laboratory Evidence of Immune Complexes in Patients on Hyposensitization Therapy. Presented, American Congress of Allergy and Immunology, New York, New York, March 27, 1977.

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: A Precision Measure of Dead Space.

WORK UNIT NO.: 76/114

PRINCIPAL INVESTIGATOR: Neal B. Kindig, Ph.D.

ASSOCIATE INVESTIGATOR: David R. Hazlett, COL, MC

OBJECTIVES

To develope a technique to measure Anatomic Dead Space during two breaths.

TECHNICAL APPROACH

The method requires a multiport valve which steers inspired and expired gas samples appropriately during a two breath test sequence. Prior to the two breath sequence an inert resident or foreign reference gas must be present in the lung. The reference gas tracks alveolar gas fluctuations. It is absent from inspired air during the two breath test. An inert gas is inspired only during the first breath of the test. The first expired sample is collected and its volume is measured. The second inspired breath contains neither test nor reference gas. The second expired sample is collected and measured.

Manpower in professional man years): 0.0

Funding (in thousands) FY 77: 0.0

PROGRESS

Dr. Kindig applied for an NiH grant to support this protocol. His application was approved but not funded.

Publications and Presentations: None

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Chemoimmunotherapy of Malignant Melanoma.

WORK UNIT NO.: 76/115

PRINCIPAL INVESTIGATOR: Nicholas J. DiBella, LTC, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To test the efficacy of BCG and BCG plus DTIC in malignant melanoma.

TECHNICAL APPROACH

Stage I - BCG by scarification weekly for 3 months, then every other week for 21 months.

Stages II & III - DTIC every 21 days with BCG on days 7, 12 and 17 of a 21 day cycle.

Manpower (in professional man years): 0.3/yr

Funding (in thousands) FY 76: 0
FY 77: 0

PROGRESS

Four patients with Stage I disease have been on the BCG program since 19 April 77 (NM), 20 April 77 (KB), 3 Dec 76 (CM) and 3 Aug 77 (DW). The only problems encountered have been marked local reactions, necessitation dose reductions in one patient.

One patient (JB) with Stage III disease has been receiving DTIC and BCG. He has been on this program since 21 Nov 76. His primary problem has been marked nausea and vomiting secondary to the DTIC; otherwise doing fine.

Another patient (JP) with Stage IV disease initially received BCG and DTIC from 22 Nov 76 to 7 Jan 77 when he was switched to BCG with methyl CCNU due to progression of metastases. By April it became evident that he had experienced only a partial response, with subsequent tumor progression. He has been removed from the study.

WORK UNIT NO.: 76/115

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: The Effect of Dexamethasone on Gonadotropins in Post-Menopausal Women.

WORK UNIT NO.: 76/116

PRINCIPAL INVESTIGATOR: Gary L. Treece, MAJ, MC

ASSOCIATE INVESTIGATOR: None.

OBJECTIVES

To clarify the mechanism whereby glucocorticoids may interfere with gonadotropin secretion or release in post menopausal women. This is of interest because of the high frequency of gonadal dysfunction in patients, male and female with endogenous as well as exogenous *Cushing's syndrome.*

TECHNICAL APPROACH

The patient population to be studied are healthy post menopausal women on no medications. A post menopausal woman will be defined as any woman with elevated plasma gonadotropin levels as a result of physiologic ovarian failure or with prior surgical extirpation of the ovaries. A baseline 0800 plasma FSH, LH and cortisol levels will be drawn on two consecutive days prior to the subjects taking 2 mg qid po of Dexamethasone on three consecutive days. A.M. FSH, LH and cortisol levels will be obtained daily during the Dexamethasone treatment. In order to define the site of the anticipated Dexamethasone suppression of the gonadotropins an LH-RH infusion test will be performed by giving a single IV bolus of 100 ug of LH-RH on the day prior to and on the third Dexamethasone treatment day. Blood for FSH and LH will be drawn at -15, 0, 15, 30, 45, 60, 90 and 120 minutes after LH-RH injection.

Manpower (in professional man years): 0.0/yr

Funding (in thousands) FY 77: 0.0

WORK UNIT NO.: 76/116

PROGRESS

Due to a delay in receiving the necessary LH-RH, an investigational drug, from Ayerst Laboratories, no progress has been made on this protocol during the interval since approval by the SGO. However, the protocol should be completed during the next fiscal year.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: A Non-Invasive Plethysmographic Measure of Transthoracic Pressure During Maximal Expiratory Maneuvers.

WORK UNIT NO.: 76/117

PRINCIPAL INVESTIGATOR: David R. Hazlett, COL, MC

ASSOCIATE INVESTIGATOR: Robert W. Zimmerer, Ph.D.

OBJECTIVES

To develop a Non-Invasive Plethysmographic method to measure Transthoracic Pressure during maximal expiratory maneuvers.

TECHNICAL APPROACH

Ten adult volunteers drawn from military and civilian staff assigned to the Pulmonary Function Laboratory will be the test population. Each individual will be subjected to Spirometry, Frequency Dependence of Functional Residual Capacity, Flow Volume Loops, Compartment Studies, Frequency Dependence of Compliance, and to Forced Vital Capacity maneuvers in the Body Plethysmograph.

Manpower (in professional man years): 0.4/yrs

Funding (in thousands) FY 77: 5.0

PROGRESS

Several measurements on each of five normal subjects have been completed. Eleven patients have also been studied as part of routine testing. The peak flow occurs within 100 milliseconds in most subjects. The flow is linear from 0 to maximum flow indicating a well defined airway resistance independent of flow rate. The shape of the curves indicate gas trapped within the lung, i.e., gas that can be compressed, but not exhaled. Preliminary measurements are related to closing volume. On many occasions, there is evidence that the airway closes completely and flow falls to 0, i.e., airways collapse at a very high speed, 100 cycles per second.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Treatment of Disseminated Carcinoma of the Breast by One of Two Standard Regimens.

WORK UNIT NO.: 77/100

PRINCIPAL INVESTIGATOR: Nicholas J. DiBella, LTC, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To determine which of two standard chemotherapy regimens for metastatic breast cancer is superior.

TECHNICAL APPROACH

Patients with metastatic carcinoma of the breast will be randomized to either CMF (cyclophosphamide, methotrexate and 5FU) or ACV (Adriamycin, cyclophosphamide and vincristine). Response rate, duration of response and survival will be monitored.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 77: 0

PROGRESS

Three patients have been treated:

1) BW is a 38 y/o WF randomized to CMF; treatment was discontinued after 8 months of therapy due to progression of osteolytic bone lesions and cutaneous metastases.

2) AH is a 65 y/o WF who was randomized to CMF, has responded and remains in complete remission after 9 months of therapy.

3) ZG is a 48 y/o WF with liver metastases, has maintained a *partial remission and remains stable on CMF for 7 months.*

Publications and Presentations: None

STATUS:

Terminated - due to the small number of patients entered on study.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME

30 SEP 77

TITLE: Evaluation of the Effects of the Frequency of Pollen Allergin Injections During the Pollen Season.

WORK UNIT NO.: 77/101

PRINCIPAL INVESTIGATOR: Lyndon E. Mansfield, MAJ, MC

ASSOCIATE INVESTIGATORS: William R. Tipton, LTC, MC
Harold S. Nelson, COL, MC

OBJECTIVES

In this investigation we hope to discover what the effect the frequency of hyposensitization injection will have in patients on maintenance level of immunotherapy during the pollen season for which they are receiving the immunotherapy.

TECHNICAL APPROACH

Two groups of patients on maintenance immunotherapy will be compared, one receiving weekly immunotherapy, the other receiving bi-weekly immunotherapy in a blinded fashion. Symptom score sheets will be completed for the course of this weed season. Nasal provocation and serum studies for levels of specific IG antibodies will be completed pre-seasonally, mid-seasonally and after the season.

Manpower (in professional man years): 0.3/yr

Funding (in thousands) FY 77: 0

PROGRESS

As of this writing twenty-two patients have been entered into this study, eleven patients in each group. Pre-seasonal challenges and tests have been obtained, mid-seasonal challenges are being completed. The patients are receiving immunotherapy in a double-blinded fashion.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Combination Chemotherapy for Extrathoracic Non-Small Cell Carcinoma of the Lung.

WORK UNIT NO.: 77/102

PRINCIPAL INVESTIGATOR: Nicholas J. DiBella, LTC, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To determine the efficacy of a four-drug chemotherapy combination for non-oat cell bronchogenic carcinoma.

TECHNICAL APPROACH

A four drug combination (bleomycin by infusion, vincristine, nitrogen mustard and adriamycin) will be tested for response, toxicity and efficacy in patients with metastatic or recurrent non-small cell cancer of the lung.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 76: 0
FY 77: 0

PROGRESS

Three patients were treated with this regimen:

1) G.M. - received three cycles without experiencing a response and with moderately severe gastrointestinal toxicity.

2) J.W. - received only one cycle of this therapy but progressed rapidly; also experienced severe gastrointestinal toxicity.

3) E.W. - received two cycles with minimal toxicity but he experienced marked anorexia and weight loss.

Publications and Presentations: None

STATUS:

Terminated - It appears to be too toxic to warrant further study in its current form.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Comparison of the Clinical and Immunological Response of Pre-Seasonal and Co-Seasonal vs. Post-Seasonal Initiation of Allergy Immunotherapy.

WORK UNIT NO.: 77/103

PRINCIPAL INVESTIGATOR: Lyndon E. Mansfield, MAJ, MC

ASSOCIATE INVESTIGATORS: William R. Tipton, LTC, MC
Harold S. Nelson, COL, MC

OBJECTIVES

To investigate in patients who present to the allergy clinic just prior to or during their symptomatic pollen season, whether it is advantageous to begin immunotherapy at that time or postpone the initiation of specific treatment until a specified period following the end of the pollen season.

TECHNICAL APPROACH

Fifteen pairs of relatively well matched new patients presenting to the allergy clinic at FAMC will undergo the usual allergy evaluation. One group of patients will have allergy immunotherapy delayed until after the season of the specific pollen has passed, with the initiation of therapy beginning one month at the end of the season, the other group will begin their allergy immunotherapy at the time the person is evaluated and within two months of the specific pollen season. A blood sample and nasal provocation testing and nasal rast testing will be performed upon initial evaluation. These procedures will be repeated just prior to the next season and immediately after the first and second pollen seasons. Patients will keep a symptom score diary during both pollen seasons.

Manpower (in professional man years): 0.0/yr

Funding (in thousands): FY 77: 0

PROGRESS

This study was not undertaken this year as we were not able to gather thirty suitable patients. The study will begin in the spring of 1978.

WORK UNIT NO.: 77/103

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Evaluation of Immunoglobulins Bearing Lymphocytes in Asthma.

WORK UNIT NO.: 77/104

PRINCIPAL INVESTIGATOR: Lyndon E. Mansfield, MAJ, MC

ASSOCIATE INVESTIGATORS: Craig Jacobson, CPT, MC
Harold S. Nelson, COL, MC

OBJECTIVES

To determine whether patients with bronchial asthma have mean immunoglobulin levels which are lower than normal for their age or have abnormalities of lymphocytes as determined by surface markers.

TECHNICAL APPROACH

All asthmatics seen in our clinic will be evaluated by means of a data sheet and will have a serum drawn for immunoglobulin studies. A subset of this group will be recontacted and have appropriate setting drawn for lymphocyte markers.

Manpower (in professional man years): 0.02/yr

Funding (in thousands) FY 77: 0

PROGRESS

One hundred thirty-five patients have been entered into the study at this time. It is expected to complete the study when two hundred patients are in the study group.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: An Evaluation of Cross Allergenicity Among Pollen Extracts of Members of Chenopodiaceae and Amaranthaceae.

WORK UNIT NO: 77/105

PRINCIPAL INVESTIGATOR: Richard W. Weber, LTC, MC

ASSOCIATE INVESTIGATOR: Harold S. Nelson, COL, MC

OBJECTIVES

To evaluate the cross allergenicity between pollens of the weed families Chenopodiaceae and Amaranthaceae, and to ascertain whether sensitivity to select members of these families can be distinguished or whether cross-reactivity with strong allergens abrogates such a discrimination.

TECHNICAL APPROACH

Twelve members of Chenopod-Amaranth families will be studied. Rabbit antisera will be raised to each weed extract and studied with Ouchterlony immunodiffusion and inhibition of passive hemagglutination. Sera collected from patients with positive skin tests will be used for RAST inhibition studies.

Manpower (in professional man years): 0.10/yr

Funding (in thousands) FY 77: 4.0

PROGRESS

Rabbit antisera have been raised to six extracts and Ouchterlony analysis performed. RAST inhibition using Russian thistle positive sera and Russian thistle discs have been done against each of the twelve extracts. Passive hemagglutination studies have not been performed to date.

Publications: None

WORK UNIT NO.: 77/105

Presentations:

(1) Weber, R.W. and Nelson, H.S.: Cross-Reactivity of Chenopod-Amaranth Weeds. Presented: Fitzsimons Pulmonary Symposium, Denver, Colorado, September 1977.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: The Effect of Chronic Non-Immunologically Mediated Bronchial Constriction of Bronchial Smooth Muscle.

WORK UNIT NO.: 77/106

PRINCIPAL INVESTIGATOR: Lyndon E. Mansfield, MAJ, MC

ASSOCIATE INVESTIGATORS: William N. Glab, SP6
John Hofmann, CPT, VC

OBJECTIVES

To determine if the hyperactivity or constriction of the bronchial smooth muscle in asthmatic patients is the cause of the bronchial smooth muscle hypertrophy found in the asthmatic lung; and secondly, to determine if bronchodilators as presently used have any protective effect against this hypertrophy.

TECHNICAL APPROACH

Guinea pigs will be subjected to non antigen mediated bronchoconstriction from the age of weaning to sexual maturity. Pulmonary functions and histological data will be obtained in depth as the guinea pigs are sacrificed.

Manpower (in professional man years): 0.0/yr

Funding (in thousands) FY 77: 1.2

PROGRESS

This study at present awaits the acquisition of the technical equipment needed to perform this study. Once this acquisition is completed the study is expected to be ongoing within the next several months before the end of calendar year 1977.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: L-Dopa Stimulation of Glucagon in Obesity.

WORK UNIT NO.: 77/107

PRINCIPAL INVESTIGATOR: Gary L. Treece, MAJ, MC

ASSOCIATE INVESTIGATOR: None.

OBJECTIVES

It has been suggested that obese subjects have a deficiency of glucagon reserve. L-Dopa is known to cause a rise in glucagon levels in normal weight subjects. This study was designed to observe the effect of L-Dopa on serum glucagon levels in obese subjects compared to normal weighted controls.

TECHNICAL APPROACH

The patient populations to be studied include 10 normal weight, non-diabetic subjects; 10 obese, non-diabetic subjects and 10 obese, diabetic subjects. In the latter group, subjects taking insulin and/or oral hypoglycemic agents will be excluded from the study. Diabetic subjects will be defined on the basis of a standard 3-hr glucose tolerance test. Subjects with a history of cardiovascular disease, glaucoma, melanoma, peptic ulcer disease, psychosis, and patients taking MAO inhibitors will be excluded from the study. All subjects will be on a weight maintaining 150 gram carbohydrate diet three days prior to the study. If not previously documented in the subject's medical records a 3-hour glucose tolerance test will be performed on a day prior to L-Dopa administration. Subsequently, after an overnight fast all will be given a 7.5 mg/kg dose of L-Dopa by mouth at 8:00 a.m. In the supine position venous blood samples will be obtained from an indwelling scalp vein catheter at -15, 0, 15, 30, 45, 60, 90, 120 and 180 minutes for determinations of plasma glucose, growth hormone, insulin, glucagon and prolactin.

Manpower (in professional man years): 0.0/yr

Funding (in thousands) FY 77: 0.0

WORK UNIT NO.: 77/107

PROGRESS

This protocol was approved by the SGO on 5 April 1977. Pending is the acquisition of scored 100 mg L-Dopa tablets necessary for making the necessary dosage increments in a variety of patients. Although no significant progress has been made on this protocol to date, completion of this protocol should be accomplished within the next fiscal year.

Publications and Presentations: None

STATUS:

Ongoing.

SURGERY

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Evaluation of Peripheral Nerve Injuries at Fitzsimons General Hospital.

WORK UNIT NO.: 71/202

PRINCIPAL INVESTIGATOR: Anthony Ballard, COL, MC

ASSOCIATE INVESTIGATOR: William W. Eversmann, Jr., LTC, MC

OBJECTIVES

The purpose of this study is to evaluate the functional recovery, sensory and motor of these upper extremity and lower extremity peripheral nerve injuries. In the past year these have been carried out by visits at Fitzsimons AMC of multiple patients who have returned at our request through our monitoring and evaluation by mail. As a consequence, long postoperative followups are being made available in order to document the long term outcome of these injuries.

TECHNICAL APPROACH

Detailed clinical and examination by electrical techniques following neurolysis and neurorrhaphy performed at Fitzsimons AMC in patients treated here since 1967 for peripheral nerve injuries continue to be the mainstay of this project. Most of the examinations are performed by the investigator or his assistant in order to maintain consistent, accurate records of prolonged followup.

Manpower (in professional man years): 0.1/yr

Funding (in thousands)	FY 76:	0
	FY 77:	0

WORK UNIT NO.: 71/202

PROGRESS

The increasing numbers of peripheral nerve injuries being seen at Fitzsimons AMC continue to be followed through the Tumor Registry type of technique of the Surgical Research Section. Our approach during the past year has been to invite increasing numbers of patients for personal examination at Fitzsimons since the questionnaire technique leaves a considerable amount to be desired from the standpoint of uniformity of examination in order to maintain comparable clinical material. Currently we are researching the possibility, because of geographical location, of outside clinics in the areas of concentrations of patients distant from Fitzsimons AMC. This work requires a detailed knowledge of geographic location of our patients which is being acquired at this time. The outside clinics might well be conducted during the course of consultant visits to MEDDAC Hospitals and/or at Veterans Administration facilities on a TDY basis. When the feasibility of this geographical location has been worked out, a supplement will be addressed to this continuing protocol. This protocol is continuing in nature.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: External Rotation Contractures in the Above Knee Amputee.

WORK UNIT NO.: 72/209

PRINCIPAL INVESTIGATOR: Anthony Ballard, COL, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To determine whether or not external rotation deformities of the proximal femur in above knee amputations create a prosthetic and ambulatory problem for the amputee.

TECHNICAL APPROACH

Plans are to study the abductor weakness created in the above knee amputee with internal and external rotation position of the hip. It is known that the intact individual external rotation weakens the abductors. The resulting gluteus medius gait is inefficient and causes increased energy expenditure.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 76: 0
FY 77: 0

PROGRESS

This original study undertaken by Dr. Gerald Mayfield has been presented to the American Academy of Orthopedic Surgeons and was well received. There is no continuing need for this study.

Publications and Presentations: None

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Treatment of Urinary Tract Trauma in the Laboratory Animal.

WORK UNIT NO.: 73/219

PRINCIPAL INVESTIGATOR: Howard E. Fauver, LTC, MC

ASSOCIATE INVESTIGATORS: Robert M. Dobbs, COL, MC

OBJECTIVES

To provide adequate training and background in the treatment of urological trauma for the urology residents, FAMC.

TECHNICAL APPROACH

1. Use of splenic bed as recipient site in autotransplantation.
2. Use of intestinal segments as temporary or permanent diversions in renal trauma.

Manpower (in professional man years): .5/yr

Funding (in thousands) FY 76: 6.0
FY 77: 6.4

PROGRESS

The project is currently between phases. Work during this year has been limited to preliminary evaluation of anestamotic techniques for urinary diversion.

WORK UNIT 73/219

Publications:

(1) Levisay, G.L.: Renal Autotransplantation in the Dog. Proc. of the Kimbrough Urological Seminar, January 1974.

(2) Jackson, J.E.: Renal Autotransplantation with Partial Nephrectomy in the Dog. Proc. of the South Central Section, AUA, Denver, Colorado, 15-19 September 1974. (Published)

(3) Page, M.E.: Renal Autotransplantation with Venal Caval Occlusion to be published in Proc. of the Kimbrough Urological Seminar, Seattle, Washington, 5 October 1975.

Presentations:

(1) Levisay, G.L.: Renal Autotransplantation in the Dog. Presented: Kimbrough Urological Seminar, Washington, D.C., January 1974.

(2) Levisay, G.L.: Renal Autotransplantation in the Dog: Presented: South Central Section Meeting of the AUA, Denver, Colorado, September 1974.

(3) Jackson, J.E.: Renal Autotransplantation with Partial Nephrectomy in the Dog. Presented: South Central Section of the AUA, Denver, Colorado, 15-19 September 1974.

(4) Jackson, J.E.: Renal Autotransplantation with Partial Nephrectomy in the Dog. Presented: Kimbrough Urological Seminar, San Antonio, Texas, 14-19 November 1974.

(5) Page, M.E.: Renal Autotransplantation with Venal Caval Occlusion to be presented at the Kimbrough Urological Seminar, Seattle, Washington, October 5, 1975.

(6) Page, M. E., and Weigel, J. W.: Exhibit-Renal Transplantation with Proximal Vena Caval. Presented: South Central Section Meeting in Urology, September 1975.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Preparation and Use of Stroma-Free Hemoglobin Solution in Hemorrhagic Shock and Cardiopulmonary Bypass Surgery.

WORK UNIT NO.: 74/201

PRINCIPAL INVESTIGATOR: Russ Zajtchuk, LTC, MC

ASSOCIATE INVESTIGATORS: George Brown, LTC, MSC
Joseph H. Baugh, COL, MC
Ben Eiseman, M.D. (Consultant)

OBJECTIVES

To develop blood substitute that will remain within the vascular space and be able to oxygenate tissues. To make the solution free of pyrogenicity and antigenicity, free from interference with typing and cross-matching, free of toxicity to visceral function, and possess a reasonable biologic half-life.

TECHNICAL APPROACH

Method of preparation of the stroma-free hemoglobin. Solution will be based on affinity chromatography. Solution will be evaluated for purity in vitro and in vivo.

Manpower (in professional man years): 3.0/yr

Funding (in thousands) FY 76: 2.0
FY 77: 0.0

PROGRESS

It was recommended that this research project be terminated due to the transfer of the principal investigator.

Publications and Presentations: None

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Treatment of Digoxin Toxicity with Activated Charcoal.

WORK UNIT NO.: 74/202

PRINCIPAL INVESTIGATOR: Donald G. Corby, COL, MC

ASSOCIATE INVESTIGATORS: John R. Hofmann, CPT, VC
Thomas P. O'Barr, PhD., DAC
W. Nicholas Glab, BS, SP/6

OBJECTIVES

Evaluate activated charcoal in the treatment of digoxin and digitoxin toxicity.

TECHNICAL APPROACH

Dogs were made digoxin or digitoxin intoxicated and subsequently treated with oral activated charcoal. Digoxin or digitoxin levels in serum, urine and bile were determined in treated and control groups.

Manpower (in professional man years): 0.3/yr

Funding (in thousands) FY 76: 0.5
FY 77: 0.5

PROGRESS

Digitoxin is presently being evaluated, as clearance of digoxin is not commensurate between man and dogs. Hepatic release via the bile, however, does occur with digitoxin in the dog, as is the case with digoxin in man. Prior to continuing the study, an adequate means of insuring digitoxic doses in the dog must be found. Additionally, it must be determined if adequate gastric motility is maintained in anesthetized dogs to supply the charcoal to the duodenum.

Publications:

(1) Zajtchuk, R.: Treatment of Digoxin Toxicity with Activated Charcoal. Am J Cardiol, Vol 35, February 1975.

WORK UNIT NO.: 74/202

Presentations:

(1) Zajtchuk, R.: Treatment of Digoxin Toxicity with Activated Charcoal. Presented: American College of Cardiology, Houston, Texas, February 1975.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Heart Valve Model Cross-Sectional Area Measurement by Electrical Impedance Technique.

WORK UNIT NO.: 74/203

PRINCIPAL INVESTIGATOR: Russ Zajtchuk, LTC, MC

ASSOCIATE INVESTIGATOR: David R. Hazlett, COL, MC
Joseph H. Baugh, COL, MC

OBJECTIVES

To improve heart valve cross-sectional area measurement.

TECHNICAL APPROACH

Impedance measurements were made at various openings and increasing hematocrit in the model. Subsequently this was done in dogs across aortic and pulmonic valves. Comparisons made between measured areas by impedance and anatomic measurements.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 76: 0.35
FY 77: 0.0

PROGRESS

Preliminary studies indicate that this method may be used in determining heart valve areas. This method appears to be more reliable than the current ways of calculating the areas i.e., Gorlin's formula. However, impedance appears to be a hyperbolic function of area and the external standard must be near the expected valve size. Experiments in cats with smaller valves had large errors similar to those seen with the Gorlin's Technique. A new catheter must be designed to overcome this fault.

WORK UNIT NO.: 74/203

Publications: None

Presentations:

(1) Hazlett, D.R., Zajtchuk, R., and Nessan, V.J.: Measuring Heart Valve Cross-Sectional Areas by an Electrical Impedance Technique. Presented: Annual Meeting of the Biomedical Engineering Society, 10-12, April, 1975, New Orleans, Louisiana.

(2) Zajtchuk, R., Hazlett, D.R., and Baugh, J.H.: Bioelectric Impedance Estimates of Heart Valve Cross-Sectional Areas. Presented: Fifth Meeting of the Association of Army Cardiology, 13-15, May, 1976.

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 82040

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Role of Hypercoagulability in Patients Undergoing Myocardial Revascularization.

WORK UNIT NO.: 75/200

PRINCIPAL INVESTIGATOR: Russ Zajtchuk, LTC, MC

ASSOCIATE INVESTIGATOR: George F. Schuchmann, LTC, MC

OBJECTIVES

To identify hypercoagulable patients undergoing saphenous vein aortocoronary bypass operations. To institute rational treatment of such patients.

TECHNICAL APPROACH

Patients undergoing coronary artery bypass surgery will be evaluated pre-operatively and on 3rd, 6th, 8th, 10th, 14th, and 21st post-operative days. Parameters which will be evaluated to include platelet count, platelet adhesivity, activated partial thromboplastin time, factor VIII assay, serum cholesterol, triglycerides, anti-thrombin III levels and lipoprotein electrophoresis. Those patients found to be hypercoagulable will be treated appropriately.

Manpower (in professional man years): 0.5/yr

Funding (in thousands)	FY 76:	3.0
	FY 77:	3.0

PROGRESS

One hundred patients undergoing coronary artery bypass graft surgery have undergone hypercoagulability screening as outlined above. Those patients found to be hypercoagulable were treated with appropriate anticoagulants. The results indicate an increased graft potency and a lower incidence of pulmonary embolism.

WORK UNIT NO.: 75/200

Publications: None

Presentations:

(1) Zajtchuk, R.: Coagulation Abnormalities in Patients Undergoing Myocardial Revascularization. The Samson Thoracic Surgical Society - 5 June 1977.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Microbial Penicillinase Antagonism to Therapy in Chronic Tonsillitis.

WORK UNIT NO.: 75/201

PRINCIPAL INVESTIGATORS: Joan E. Zajtchuk, LTC, MC
George L. Brown, LTC, MSC

ASSOCIATE INVESTIGATORS: William H. Falor Jr., MAJ, MC

OBJECTIVES

To determine whether refractoriness in penicillin therapy in chronic tonsillitis is due to local penicillinase production or whether this is an anatomic basis.

TECHNICAL APPROACH

The following study was undertaken in patients with chronic tonsillitis to determine if local penicillinase production occurred within the tonsillar crypts, or if an anatomic nucleus for the proliferation of bacteria existed.

Crypt and surface cultures of patients who have chronic tonsillitis and are scheduled for tonsillectomy are studied for microbial flora including bioassays for penicillinase. Patients who are treated with penicillin for clinical reasons will be compared with the non-treated group. Tonsil homogenates will also be studied.

Manpower (in professional man years): 0.5/yr

Funding (in thousands) FY 76: 2.5
FY 77: 0

PROGRESS

The project was terminated at 2 years in November 1976 and the data are being analyzed. These data will be submitted for publication or presentation.

WORK UNIT NO.: 75/201

PROGRESS - continued

There appears to be no local penicillinase production within the tonsillar crypts. There is a higher incidence of culture positive pathogens within the crypts which may act as a reservoir and account for the repeated recurrences of actual episodes of tonsillitis.

Publications and Presentations: None

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: The Wet Lung 1: Solubility of Inert Gases in Lung Tissue and Blood.

WORK UNIT NO.: 75/202

PRINCIPAL INVESTIGATOR: Russ Zajtchuk, LTC, MC

ASSOCIATE INVESTIGATORS: David Hazlett, COL, MC
Robert E. Yancy, CPT, MSC

OBJECTIVES

To determine the solubility of certain inert gases in lung tissue and blood.

TECHNICAL APPROACH

Tissue homogenate or blood will be deaerated in a manometric Van Slyke chamber and then transferred anaerobically to a tonometer through which the desired inert gas is flowing. After equilibration the solubility of gas will be determined with Van Slyke apparatus. The Bunsen solubility coefficient will be calculated.

Manpower (in professional man years): 0.2/yr

Funding (in thousands) FY 76: 1.0
FY 77: 0.0

PROGRESS

Technique has been worked out and data collection begun. The Bunsen solubility coefficient for lung and liver is .416 and .229 respectively which is in reasonable agreement with published data. CPT R.E. Yancy has had a great deal of technical difficulty but has developed the techniques sufficiently to carry out measurement when and if we obtain a CVP mass spectrometer.

Publications and Presentations: None

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Treatment of Renal Trauma in Laboratory Animals.

WORK UNIT NO.: 76/201

PRINCIPAL INVESTIGATOR: Torrence M. Wilson, MAJ, MC

ASSOCIATE INVESTIGATORS: Robert M. Dobbs, COL, MC
Howard E. Fauver, LTC, MC

OBJECTIVES

Investigation of treatment of central renal trauma with extracorporeal surgery and autotransplantation of the repaired kidney.

TECHNICAL APPROACH

Mongrel dogs will have the central portion of a kidney resected segmentally using microdissection extracorporeally. Renal autotransplantation to the animal's pelvis will then be done, anastomosing the renal vessels to the iliac vessels: renal artery end to end to iliac artery, and renal vein end to side to iliac vein. Spot urine and blood creatinine, urea, and sodium will be collected preoperatively. At sacrifice, samples for above chemistries will be collected.

Manpower (in professional man years): 0.5/yr

Funding (in thousands) FY 76: 2.0
FY 77: 2.0

PROGRESS

To date 27 operations have been performed. Limited success has been encountered, with two dogs cancelled for multiple renal vessels. Six operations have been successful.

Publications and Presentations: None

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: An Experimental Dog Model for the Study of Coronary Artery Spasm.

WORK UNIT NO.: 76/202

PRINCIPAL INVESTIGATOR: George F. Schuchmann, LTC, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To establish an animal model for the study of coronary artery spasm and to study the effects of various drugs on coronary artery blood flow.

TECHNICAL APPROACH

Surgical details of the IMA-RCA grafts have been well worked out. Flow probe measurements as outlined in the protocol continue to be inaccurate and have delayed data collection.

Manpower (in professional man years): 0.1/yr

Funding (in thousands)	FY 76:	1.0
	FY 77:	1.0

PROGRESS

Five dogs were long-term survivors of IMA-RCA grafts. All dogs had patent grafts proven by angiography. Later, all dogs were sacrificed and all grafts found patent at the time of surgery. Unfortunately, flow probe difficulties made collection of meaningful flow data impossible. This experiment is currently inactive while a means of obtaining accurate flow measurements is obtained.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Screening Program for Military Children at High Risk for Hearing Loss.

WORK UNIT NO.: 76/203

PRINCIPAL INVESTIGATOR: Susan T. Slibeck, M.S., DAC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To screen infants and children for information indicating high risk for hearing loss so that early identification and treatment can be enhanced.

TECHNICAL APPROACH

Red Cross volunteers will screen the medical and family histories of all newborns, pediatric ward patients (0-6 years of age), and one-year old Well Baby Clinic patients through parent interviews and chart reviews. The investigator will review the gathered data for indications of high risk for hearing loss and designate children as AT RISK or NOT AT RISK. AT RISK children will be tested by an audiologist periodically for one year or until hearing loss is ruled out.

Manpower (in professional man years): 0.0

Funding (in thousands) FY 77: .5

PROGRESS

This report covers the eight and one-half month active period of the High Risk Registry screening program (17 October 1976 to 31 June 1977). During that time 408 children were screened by three Red Cross volunteers; 169 of these children were considered AT RISK for hearing loss; and 111 children are currently being followed on the Registry as indicated.

WORK UNIT NO.: 76/203

PROGRESS - continued

Four children with depressed auditory acuity were identified. Audiometric testing and otologic consultation indicated significant hearing loss due to middle ear fluid, middle ear infection, or excessive cerumen. At the time of the screening these hearing/medical problems had not been previously identified. One of the four children also had a significant sensorineural loss requiring amplification with a hearing aid and special rehabilitation intervention. The ages of the four children ranged from 6 months to 2 years; thus achieving the objective of early identification and treatment.

The value of High Risk Registers is well documented: "Infants at risk for hearing impairment should be identified by means of history and physical examination" (National Joint Committee on Newborn Hearing Screening, 1973). The committee found that a High Risk Registry can increase identification of hearing impairment as much as tenfold. Reports of similar registers indicate that 1 out of 57 AT RISK children will be hearing impaired. The registry procedures used in this program have yielded a more economical result: 1 out of 42 AT RISK children were hearing impaired.

Publications: None

Presentations:

(1) Slibeck, Susan T.: High Risk Factors for Hearing Loss. Presented: Pediatrics Department, Fort Carson, Colorado, December 1976.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: The Role of Hypercoagulation in Neurosensory Hearing Loss in Guinea Pigs.

WORK UNIT NO.: 76/204

PRINCIPAL INVESTIGATOR: Joan T. Zajtchuk, LTC, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

This protocol is designed to determine whether producing a hypercoagulable state of an acute or chronic nature in guinea pigs can result in a neurosensory hearing loss. Hearing thresholds in animals made hypercoagulable by the infusion of a l-homocystine solution or by hypertransfusion will be compared to normal controls. Hearing levels will be recorded with a transtympanic pick-up electrode on the promontory of anesthetized guinea pigs. Eight nerve action potentials and cochlear microphonic recordings will be computer averaged for each experimental situation.

TECHNICAL APPROACH

Sudden hearing loss is defined as deafness which occurs in an instant or develops very rapidly over a few days. In a series of fourteen patients seen by the Fitzsimons Army Medical Center Otolaryngology Service with a history of sudden hearing loss, nine were found to be hypercoagulable. Using this clinical observation, it is suggested that an abnormal coagulation state could produce a sudden neurosensory hearing loss. The aim of this experiment is to prove this hypothesis in guinea pigs. If it is found that a hypercoagulable state is responsible for cochlear damage, then the use of anticoagulants in these individuals may reverse their hearing loss or protect them from further hearing loss.

Manpower (in professional man years): 0.0

Funding (in thousands) FY 77: 0.0

PROGRESS

Definitive work was never begun on this research. The principal investigator has been transferred to WRAMC.

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Use of Cyclic AMP in the Evaluation of Calcium Urolithiasis.

WORK UNIT NO.: 76/205

PRINCIPAL INVESTIGATOR: Robert M. Dobbs, COL, MC

ASSOCIATE INVESTIGATOR: James B. Haden, MAJ, MC

OBJECTIVES

The use of nephrogenous Cyclic-AMP in the evaluation of stone disease.

TECHNICAL APPROACH

The use of various blood studies and urine collections to define the metabolic basis of stone disease in recurrent stone formers. The hallmark of these studies will be serum and urine cyclic AMP. Using these values, appropriate treatment will be prescribed to patients.

Manpower (in professional man years): .25/yr

Funding (in thousands) FY 77: .3

PROGRESS

Over 125 patients have been evaluated via the stone protocol and currently being followed and treated based on our results. Currently, the department of endocrinology will further assist in this evaluation. As an offshoot of the original stone protocol, stone workups are being standardized and treatment better understood especially with the use of nephrogenous Cyclic-AMP. Recently we have also started an early program in the detection of prostaglandin activity in stone disease.

Publications:

(1) Haden, J.B.: Ambulatory Evaluation of Stone Disease. Proceedings of Kimbrough Urological Seminar, San Diego, California, October 1976.

WORK UNIT NO.: 76/205

Presentations:

(1) Haden, J.B.: Ambulatory Evaluation of Stone Disease. Kimbrough Urological Seminar, San Diego, California, October 1976.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Electrocochleography: An Objective Measurement of Hearing Thresholds.

WORK UNIT NO.: 76/206

PRINCIPAL INVESTIGATOR: Joan E. Zajtchuk, LTC, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To determine an accurate objective measurement of hearing by recording the action potential from the VIIIth cranial nerve in response to sound stimulation of varying intensities and frequencies.

TECHNICAL APPROACH

Most of the efforts of this work could be directed toward the early detection and identification of hearing loss in infants. The important period of language development can be fully utilized by early aiding and special schooling in the hearing impaired child. Conventional audiometry would first be done. Infants who do not give clearly defined hearing thresholds would be candidates for a special test procedure using a needle electrode 0.2 mm in diameter which is inserted through the tympanic membrane and positioned against the promontory by an otolaryngologist.

Manpower (in professional man years): 0.0

Funding (in thousands) FY 77: 0.0

PROGRESS

It was recommended that this research project be terminated due to the transfer of the principal investigator. There are no plans to continue this protocol here at FAMC.

Publications and Presentations: None

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE Investigation of Ureter (Partial and Complete) and Bladder (Sub-total) Replacement with Synthetic Materials.

WORK UNIT NO.: 77/200

PRINCIPAL INVESTIGATOR: Torrence M. Wilson, MAJ, MC

ASSOCIATE INVESTIGATORS: Robert M. Dobbs, COL, MC
Norman E. Peterson, M.D., Chief, Urology Service
University of Colorado Medical School

OBJECTIVES

Evaluate the feasibility of replacing ureteral segments and bladder segments with synthetic prosthetic devices. The initial effort will be with Gor-Tex.

TECHNICAL APPROACH

Mongrel dogs under anesthesia will have a portion of their ureter or bladder replaced with Gore-Tex. Followup evaluation will include contrast studies and tissue segments for pathologic study.

Manpower (in professional man years):

Funding (in thousands): FY 77:

PROGRESS

Project just initiated. No results to report yet.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Hydrodynamic Studies With a New Cardiac Bivalve Prosthesis and Comparison with Currently Used Prosthesis in a Pulse Duplicator.

WORK UNIT NO.: 77/201

PRINCIPAL INVESTIGATOR: Alan E. Seyfer, MAJ, MC

ASSOCIATE INVESTIGATOR: David R. Hazlett, COL, MC

OBJECTIVES

To compare cardiac valvular prosthesis with a new, low-profile, low-gradient, bivalve prosthesis.

TECHNICAL APPROACH

Inspite of tremendous advances in heart valve prosthesis, there continues to be a need for a low-profile, low-gradient, central-flow heart valve substitute. It is the purpose of this investigation to study a new cardiac valve with these specifications and to test the prototype of such a valve in a pulse duplicator. The tests will be conducted according to a strict physiologic protocol which was described in the recently submitted project outline.

Manpower (in professional man years): 0.10/yr

Funding (in thousands) FY 77: 5.0

PROGRESS

During the current fiscal year, study on this project has concentrated mainly in the design and construction of a prototype cardiac prosthesis. Although several models of the original prototype design have been completed, these models were constructed out of cheap, nondurable substances in anticipation of correctable design problems. Currently, a final design prototype for insertion in the pulse duplicator is being constructed. Likewise, we are awaiting the arrival of the necessary equipment to conduct the experiments.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATIONS

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Comparison of Metabolic and Functional Changes in Defects of Platelet Function.

WORK UNIT NO.: 72/302

PRINCIPAL INVESTIGATOR: Donald G. Corby, COL, MC

ASSOCIATE INVESTIGATORS: T.P. O'Barr, Ph.D., DAC
Judy A. Barber, B.S., DAC
Wayne Goad, M.A., DAC

OBJECTIVES

To correlate biochemical and functional parameters to gain a better understanding of the pathophysiology of functional or qualitative platelet disorders.

TECHNICAL APPROACH

Platelet function studies (aggregation, adhesion, and adenine nucleotide AN) content and the release of these compounds following aggregation with collagen and epinephrine will be measured in patients with various congenital and acquired disorders of platelet function. These results will be correlated with appropriate metabolic studies: adenyl cyclase, c-AMP, prostaglandin endoperoxides (thrombozanes A_2 and B_2), membrane glycoproteins, etc. In addition membrane receptors for epinephrine will be quantitatively evaluated using a new technique of binding with radioactive dihydroergocryptine. Other metabolic studies will be added as indicated.

Manpower (in professional man years): 0.25/yr

Funding (in thousands)		
	FY 76:	0.5
	FY 77:	4.5

PROGRESS

During the past fiscal year, work on this project has concentrated in further investigation of the qualitative abnormality of platelets of newborn infants. In earlier studies (Corby & Schulman, J. Ped. 79:307, 1971) we showed that the platelets of newborn infants fail

WORK UNIT 72/302

PROGRESS - continued

to aggregate normally in response to a variety of inducers of platelet function which promote the release of adenosine diphosphate from the platelet. Data derived from FAMC Clinical Investigation Protocol 71/301 (completed in FY 75) suggested that this impairment of ADP release was due to a decreased sensitivity of newborn platelets to external stimuli (collagen and epinephrine). Since the importance of prostaglandin endoperoxides, prostaglandin G2, (PGG_2) in mediating the release of ADP from the platelets has recently been established, it appeared necessary to determine if the metabolic pathway leading to the formation of these prostaglandin endoperoxides was functional in newborn platelets. The results of these studies, reported at the 6th International Congress on Thrombosis and Hemostasis in Philadelphia, Pennsylvania, June of 1977, are described in the following abstracts: Cyclooxygenase activity was evaluated in washed platelets from paired mother and cord blood samples by monitoring the incorporation of radioactivity into metabolites during incubation with (1-^{14}C) arachidonic acid. Thin layer radiochromatograms of methylated incubation products were essentially identical. Three main peaks of radioactivity, which corresponded to identified arachidonic acid metabolites, were noted (Malmsten et al. Proc. Natl. Acad. Sci., USA, 72:1446-1450, 1975). Platelets from mothers and newborns incorporated similar amounts of radioactivity into 8-(1-hydroxy-3-oxopropyl)-9, 12L-dihydroxy-5-10-heptadecadienoic acid (PHD) and 12L-hydroxy-5,8, 10-heptadecatrienoic acid (HHT). Some variation in the extent of aggregation to arachidonic acid was observed in individual PRP samples from both mothers and infants. All infants studied exhibited aggregation in response to 50 ug of arachidonic acid. Aspirinated adult platelets, in which the conversion of arachidonic acid to prostaglandin endoperoxides is blocked, were mixed with an equal volume of newborn platelets which had been shown to be refractory to collagen and epinephrine. Although no correction was noted when epinephrine was used as the inducing agent, marked aggregation was observed following the addition of 0.1 mg/ml of soluble collagen.

The normal aggregation of newborn platelets, demonstration of the formation of prostaglandin endoperoxide metabolites, PHD and HHT, indicate that the cyclo-oxygenase pathway is intact in newborn platelets. The demonstration of correction of second phase aggregation found after administration of soluble collagen in the mixtures of aspirinated adult and normal newborn platelets further suggest that the sufficient quantities of endogenous arachidonic acid can be made available by the action of phospholipase on membrane phospholipase on membrane phospholipids. The variability of this response as noted by the failure to form adequate amounts of prostaglandin G2

WORK UNIT 72/302

PROGRESS - continued

after stimulation by epinephrine further suggests that the newborn platelet abnormality might reside in decreased sensitivity of its "Membrane Receptor Sites" to inducers of platelet function. Further work in this project (begun Sept 1977) will concentrate on evaluating membrane receptor sites for epinephrine using binding with ^{3}H-dihydroergocryptine and quantitative and characterizing membrane phospholipids and glycoproteins.

Publications:

(1) Corby, D.G., Shigeta, F.H., Greene, H.L., and Stifel, F.B.: Platelet Dysfunction in Glycogen Storage Disease Type I (GSDI): Reversal with Total Parenteral Alimentation (TPA). (Abst.) Clin. Res. 21:304, 1973.

(2) Corby, D.G., Preston, K.A., Shigeta, F.H., O'Barr, T.P., and Zuck, T.F.: Adverse Effect of Gel Filtration on the Adenine Nucleotides of Human Platelets. (Abst., P. 107), III Congress, International Society on Thrombosis Hemostasis (Vienna, Austria), June 1973.

(3) Corby, D.G., (Intr. by Wm. E. Hathaway): Mechanism of Platelet Dysfunction in Newborn Infants. J. Ped. Res., Vol. 8, No. 4, April 1974.

(4) Corby, D.G., Preston, K.A., O'Barr, T.P.: Adverse Effect of Gel Filtration on the Function of Human Platelets. Proceedings of the Society for Experimental Biology and Medicine, 146:96-98, 1974.

(5) Corby, D.G., Putnam, C.W., Greene, H.L.: Impaired Platelet Function in Glucose-6-Phosphatase Deficiency. The J. Ped., 85:71-76, July 1974.

(6) Corby, D.G., and Zuck, T.F.: Newborn Platelet Dysfunction: A Storage Pool and Release Defect. Thrombosis and Haemostasis, 36:200-207, 1976.

(7) Corby, D.G., Goad, W.C., Barber, J., and O'Barr, T.P.: Evaluation of Cyclo-Oxygenase Pathway in Platelets of the Newborn, Thrombosis and Haemostasis (Stuttgart), 38:35, 1977 (Abstract).

WORK UNIT NO.: 72/302

Presentations:

(1) Corby, D.G., Shigeta, F.H., Greene, H.L., and Stifel, F.B.: Platelet Dysfunction in Glycogen Storage Disease Type I (GSDI): Reversal with Total Parenteral Alimentation (TPA). Presented: Western Society for Pediatric Research, Carmel, California, February 1973.

(2) Corby, D.G., Preston, K.A., Shigeta, F.H., O'Barr, T.P., and Zuck, T.F.: Adverse Effect of Gel Filtration on the Adenine Nucleotides of Human Platelets. Presented: III Congress, International Society on Thrombosis and Hemostasis, Vienna, Austria, June 1973.

(3) Corby, D.G.: Mechanism of Platelet Dysfunction in Newborn Infants, Society for Pediatric Research, APS-SPR, Washington, D.C., May 1974.

(4) Corby, D.G., Goad, W.C., Barber, J., and O'Barr, T.P.: Evaluation of Cyclo-Oxygenase Pathway in Platelets of the Newborn. Presented: VIth International Congress on Thrombosis and Haemostasis, Philadelphia, Pennsylvania, June 1977.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Computer Storage and Analyses of Mycobacteriologic Laboratory Data from Tuberculous Patients.

WORK UNIT NO.: 73/305

PRINCIPAL INVESTIGATORS: George L. Brown, LTC, MSC, Ph.D.
James J. Damato, MAJ, MSC

ASSOCIATE INVESTIGATORS: Mary V. Rothlauf, M.S., DAC
Al Bell, DAC

OBJECTIVES

To establish and maintain an in-depth data base of mycobacteriological data on FAMC tuberculosis service patients.

TECHNICAL APPROACH

Since 1968 all mycobacteriologic results on FAMC tuberculosis patients have been stored in a computer file. Presently 2524 patient records encompassing 55,772 messages have been accumulated in the computer file. Patient data include: smear and culture results, drug susceptibilities of mycobacterial isolates, initial drug therapy data, serum tests, data on special study patients, and experimental data on methodology studies.

Manpower (in professional man years): 1.0/yr

Funding (in thousands)		
	FY 76:	1.5
	FY 77:	1.5

PROGRESS

Between September 1976 and September 1977, 274 patients were studied; a total of 3272 additional messages were incorporated in the existing computer file. The Formated File Print encompassing nine (9) options is presently operational:

WORK UNIT 73/305

PROGRESS - continued

1. Entire file print; 2. Supplementary patient identification; 3. Culture report; 4. Serum inhibition/drug level report; 5. Patient therapy report; 6. Organism identification; 7. Period (time span) report; 8. Individual patient print; 9. Sex-race retrieval.

Computer file analyses of contamination data from 1 January 1972 - 31 December 1976 shows decline of contamination rates with the incorporation of Mitchison's Selective 7H10 OA (PACT) medium; previous average, 3.5% annual contamination rate: current average, 1.6% annual contamination rate.

Publications: None

Presentations:

(1) Brown, G.L, and M.V. Rothlauf: Laboratory Management of the Tuberculous Patient. Computer File Analyses of Six Year Data. Society of Armed Forces Laboratory Officers, San Antonio, Texas, September 1976.

(2) Brown, G.L., and M.V. Rothlauf: Computer Utilization in the Laboratory. Colorado State University, Ft. Collins, Colorado, April 1977.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Microbiological Research in Tuberculosis.

WORK UNIT NO.: 74/300

PRINCIPAL INVESTIGATORS: George L. Brown, LTC, MSC, Ph.D.
James J. Damato, MAJ, MSC

ASSOCIATE INVESTIGATORS: Mary V. Rothlauf, M.S., DAC
James D. Hakes, DAC

OBJECTIVES

To evaluate and/or design new methods for improving diagnostic laboratory procedures in mycobacteriology and to maintain an in-depth data base of laboratory results on tuberculous patients.

TECHNICAL APPROACH

Continuing projects are designed to use clinical materials from FAMC tuberculosis service patients. Specific studies under this project: (I) Comparison of Middlebrook 7H11 OA Agar with Modifications thereof, in an effort to improve isolation of mycobacteria from clinical specimens; (II) Tests for identification of mycobacterial species; (III) Evaluation of drug susceptibility test medium.

Manpower (in professional man years): 0.5/yr

Funding (in thousands) FY 76: 1.6
FY 77: 1.6

PROGRESS

Evaluation of the media comparison data has shown that the Mitchison's selective OA agar (PACT) is a medium of choice for isolation of mycobacteria from raw clinical specimens. This is evident where small numbers of organisms are involved and also in the isolation of mycobacteria other than M. tuberculosis (Mott), particularly Runyon Groups I and III. Data from the media comparison study are being prepared for publication.

WORK UNIT 74/300

PROGRESS - continued

Comparison of the data since routine use of PACT was adapted, shows a dramatic reduction in contamination rate with the use of the selective medium. This information will be added to the media comparison data in preparation for publication.

B-glucosidase activity of mycobacteria was evaluated for its incorporation in the battery of tests used to speciate mycobacteria. It was found that p-nitrophenyl-B~D Glucoside (PNPG) test is a simple procedure and can be used for the differention of M. tuberculosis from other mycobacteriae.

A pilot study comparing PACT as a base medium and routine medium for drug susceptibility studies indicated that for direct determination the correlation of the PACT with routine medium is excellent. Evaluation of these two types of media is ongoing based on specimen availability.

Publications:

Kolb, J.G., Rothlauf, M.V., and G.L. Brown: Isolation of Mycobacterium kansasii on Michison's Selective 7H11 medium. (Abstract) American Society for Microbiology, C-69:47, 1977.

Presentations:

Kolb, J.G., Rothlauf, M.V., and G.L. Brown: Isolation of Mycobacterium kansasii on Mitchison's Selective 7H11 Medium. American Society for Microbiology, New Orleans, Louisiana, May 1977.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: The Depletion of Liver Glycogen During Endotoxemia.

WORK UNIT NO.: 74/303

PRINCIPAL INVESTIGATOR: Thomas P. O'Barr, Ph.D., DAC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To examine the possibility that the hypoglycemic state present in endotoxin-poisoned animals results from the over production of insulin.

TECHNICAL APPROACH

Two hundred gram Holtzman rats, which were injected eighteen hours prior to use with saline or 100 ug of Salmonella Typhimurium endotoxin, were anesthetized with pentobarbital, and the pancreas prepared for perfusion according to the technique of Sussman et al. (Metabolism 13:466-476, 1966). Various concentrations of glucose were perfused through the organ and the effulent examined for immunoreactive insulin.

Manpower (in professional man years): 0.1/yr

Funding (in thousands)		
	FY 76:	0.5
	FY 77:	0.0

PROGRESS

No progress was made during this fiscal year.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Clinical Application of TSH Radioimmunoassay.

WORK UNIT NO.: 74/305

PRINCIPAL INVESTIGATOR: Robert A. Adler, MAJ, MC

ASSOCIATE INVESTIGATORS: T.P. O'Barr, Ph.D., DAC
Nassar Ghaed, LTC, MC

OBJECTIVES

To establish a specific homologous radioimmunoassay for thyrotropin, TSH.

TECHNICAL APPROACH

The radioimmunoassay developed uses anti-human TSH material from the NIH. TSH standard used is from the Medical Research Council in England. 125-I is attached to standard TSH via a Sephadex Column method and chloramine T.

Manpower (in professional man years): .25/yr

Funding (in thousands) FY 76: 4.0
FY 77: 0.0

PROGRESS

An operational RI assay for TSH has been developed. Due to the departure of the principal investigator the study is completed.

Publications:

(1) Adler, R.A., Bergin, J.J., and O'Barr, T.P.: Clinical Use of Serum Thyrotropin (TSH) Radioimmunoassay: The Low Thyroid Reserve Syndrome, (in preparation).

WORK UNIT NO.: 74/305

Presentations:

(1) Adler, R. A., Bergin, J. J. and O'Barr, T. P: Clinical Use of Serum Thyrotropin (TSH) Radioimmunoassay: The Low Thyroid Reserve Syndrome, Regional Meeting of the American College of Physicians, Colorado Springs, Colorado, 15 January 1976.

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Effect of Oral Water Loading on Plasma Prolactin.

WORK UNIT NO.: 75/300

PRINCIPAL INVESTIGATOR: Robert A. Adler, MAJ, MC

ASSOCIATE INVESTIGATOR: T. P. O'Barr, Ph.D., DAC

OBJECTIVES

To further clarify the effect of oral water loading on plasma prolactin secretion in various clinical states.

TECHNICAL APPROACH

Normal patients, pituitary tumor patients, people with idiopathic cyclicedema, and patients with drug-induced hyperprolactinemia will be tested for prolactin response to an oral water load. Prolactin is measured by radioimmunoassay.

Manpower (in professional man years): 0.1/yr

Funding (in thousands)	FY 76:	3.0
	FY 77:	0.0

PROGRESS

Due to the resignation of the principal investigator, no further patients were entered into the study.

Publications:

(1) Adler, R.A., Noel, G.L., Wartofsky, L., Frantz, A.G.: Failure of All Water Loading and Intravenous Hypotonicsaline to Suppress Plasma Prolactin in Man, J. of Clin. Endocrinol. 41:383, 1975.

(2) Hofeldt, F.D., Adler, R.A., Boland, M.J., Block, M.B.: Galactorrhea: What Does It Mean? Rocky Mountain Medical Journal 73:252, 1975.

WORK UNIT 75/300

Publications - continued

(3) Adler, R. A.: The Evaluation of Galactorrhea. Am J Obstet Gynecol. 127:569-571, 1977.

Presentations: None

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FTIZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Circulatory and Hormoral Changes In Dogs During Acute Pancreatitis.

WORK UNIT NO.: 75/301

PRINCIPAL INVESTIGATOR: William L. Daniels, CPT, MSC

ASSOCIATE INVESTIGATORS: John G. Miller, CPT, VC
Thomas P. O'Barr, Ph.D., DAC
James A. Seab, Jr., MAJ, MC

OBJECTIVES

To determine changes that occur in heart rate, blood pressure, plasma glucagon, plasma insulin, blood glucose and serum amylase during the development of acute pancreatitis. To determine the effect of drugs, suggested for use in treatment of acute pancreatitis, on the above parameters and on the development of acute pancreatitis.

TECHNICAL APPROACH

a) Acute pancreatitis is induced by injection of 10 cc. of autologous bile into the dorsal pancreatic duct.

b) 5-fluorouracil and Aprotinin will be given in two groups of dogs at the time of induction of pancreatitis.

c) Blood pressures and electrocardiograms will be recorded.

d) Blood samples will be drawn hourly to measure plasma glucagon, plasma insulin, serum amylase, and serum glucose.

Manpower (in professional man years): 0.2/yr

Funding (in thousands)		
	FY 76:	2.0
	FY 77:	0.0

PROGRESS

Due to the departure of the principal investigator from FAMC, no further work was done on this study.

WORK UNIT NO.: 75/301

PROGRESS - continued

Publications:

(1) Daniels, W. L., O'Barr, T. P., Miller, J. G., and Seab, J.: Circulatory and Hormonal Changes During Acute Pancreatitis. Fed. Proc., Vol. 35, No. 3, 1976. Abstract No. 1035.

Presentations:

(1) Daniels, W. L., O'Barr, T. P., Miller, J. G., and Seab, J.: Circulatory and Hormonal Changes During Acute Pancreatitis. Federation Proceedings, April 1976.

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Immuno-Surveillance Monitoring in Post Surgery Cancer Patients as Means of Evaluating Anti-Tumor Response.

WORK UNIT NO.: 75/303

PRINCIPAL INVESTIGATOR: George L. Brown, LTC, MSC

ASSOCIATE INVESTIGATORS: Joseph H. Baugh, COL, MC
Richard M. Hirata, COL, MC

OBJECTIVES

To evaluate tumor cell-mediated immunity and immuno-surveillance mechanisms in breast and colorectal cancer patients post-operative at different stages of disease.

TECHNICAL APPROACH

About 10-20 cc heparinized and clotted blood samples are obtained at the time of surgery; when available, 1-3 gm of tissue from the excised tumor is also obtained. Additional heparinized and clotted blood samples are obtained at monthly intervals. Soluble tumor components are extracted from tumor by standard technique and are used as stimulants on lymphocytes. Serum samples are evaluated for immunoglobulin content (i.e., IgG, IgM, IgA, alpha 1 glyco-protein), serum protein electrophoretic profiles, and carcinoembryonic antigen. Cellular immuno mechanism is also evaluated monthly after surgery by lymphocyte blast transformation technique using mitogenic stimulation with phytohemogglutinin, conconavalin A and pokeweed mitogen. Peripheral lymphocytes are quantitated as to percent thymic derived lymphocyte population with SRBC "rosette" test.

Manpower (in professional man years): 1.5/yr

Funding (in thousands)		
	FY 76:	2.0
	FY 77:	2.0

PROGRESS

A total of 24 patients encompassing eleven (11) breast and thirteen (13) colon cancer types were studied for periods of two to eleven months. Period of evaluation started on date of surgery with monthly follow-up intervals. Approximately 50% of the patients, in addition to indicated

WORK UNIT NO.: 75/303

PROGRESS - continued

surgical procedures, were also placed on selected chemotherapy. Serum evaluations for IgG, IgM, IgA, complement C'3 and C'4, and electrophoretic profile showed no abnormal results. Concentrations of serum alpha 1 acid glycoprotein in 70-75% of subjects were elevated on the initial sample with normalization within two (2) months post surgery. Two (2) patients with clinical metastatic symptoms were noted to have elevated alpha 1 acid glycoprotein. Lymphocyte blast transformation post mitogenic stimulation was suppressed on the initial samples, date of surgery, with normalization within two months. No differences in lymphocyte blast transformation were noted in the non-chemotherapeutic treated and treated groups.

Publications:

Brown, G.L., DiBella, N., and D.G. Corby: IgE-IgM kappa Gammopathy Associated with Lymphocytic Lymphoma: Immunological Evaluation. Military Medicine, 1977 (December issue).

Presentations:

Brown, G.L.: Immuno-Surveillance of the Cancer Patient: Laboratory Parameters. Colorado State University, Ft. Collins, Colorado, July 1977.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: 24-Hour Prolactin Patterns in Patients with Galactorrhea and/or Pituitary Tumors.

WORK UNIT NO.: 75/304

PRINCIPAL INVESTIGATOR: Robert A. Adler, MAJ, MC

ASSOCIATE INVESTIGATORS: Stephen R. Plymate, MAJ, MC
T. Philip O'Barr, Ph.D., DAC

OBJECTIVES

This study attempts to find a new tool for differentiating functional from tumor-induced galactorrhea and for assessing pituitary function in patients with pituitary tumors and/or hypogonadism.

TECHNICAL APPROACH

Samples for hormones are drawn every 20 minutes through an indwelling catheter via a constant withdrawal pump connected to a fraction collector. The following hormones are measured by sensitive and specific radioimmunoassays: prolactin (PRL), follicle stimulating hormone (FSH), luteinizing hormone (LH), and testosterone (T). The assay for Estradiol (E_2) is under development.

Manpower (in professional man years): 2/yr

Funding (in thousands)	FY 76:	4.0
	FY 77:	0.0

PROGRESS

Due to the resignation of the principal investigator, no further patients were entered into the study.

WORK UNIT NO.: 75/304

Publications:

(1) Adler, R. A.: The Evaluation of Galactorrhea. Am J Obstet Gynecol. 127:569-571, 1977.

Presentations:

(1) Adler, R. A.: Prolactin, 1976, Endocrine Grand Rounds, University of Colorado Medical School, Denver, Colorado, 15 January 1976.

(2) Adler, R. A.: Prolactin, 1976, Endocrine Research Seminar, Dartmouth Medical School, Hanover, New Hampshire, 9 April 1976.

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Mechanisms of Vitamin D Induced Calcium Transport.

WORK UNIT NO.: 76/300

PRINCIPAL INVESTIGATOR: Art Charles, LTC, MC

ASSOCIATE INVESTIGATOR: Phil O'Barr, Ph.D., DAC

OBJECTIVES

Futher characterization of vitamin D induced transcriptional event as it relates to calcium transport processes on polar cells.

TECHNICAL APPROACH

The isolation of mRNA involving proteins thought to be related in calcium transport by gel and chromatographic methods.

Manpower (in professional man years): .0 yr

Funding (in thousands) FY 77: .5

PROGRESS

Because of manpower shortages this protocol has been unable to be started.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Pancreatic Islet Transplantation in Diabetic Animals.

WORK UNIT NO.: 76/301

PRINCIPAL INVESTIGATOR: Art Charles, LTC, MC

ASSOCIATE INVESTIGATORS: George L. Brown, LTC, MSC
Phil O'Barr, Ph.D., DAC
John Hofmann, CPT, VC

OBJECTIVES

Information derived from islet transplantation experiments indicates that diabetes mellitus can be effectively treated in animals. For this treatment approach to become practical in humans it appears obligatory to achieve effective animal autologus islet transplants. This goal has not been realized and thus the current protocol directly attempts to perform autologus islet transplantation in diabetic animals.

TECHNICAL APPROACH

Rat colonies of three different varieties, Lewis, Wistar Furth, and Fischer strains have been established at FAMC. The Lewis and Fischer strains share major rat histocompatibility antigens whereas Wistar Furth does not. Pancreatic islets are isolated and purified from donor strain animals and under various conditions are transplanted to Lewis recipients. The assessment of transplantation success is made by measurement of daily urine volumes and 24-hour urine glucose excretion in addition to serum glucose values. Immunological studies of the transplantation are performed by immunization of rabbits by rat islet antigen from crude islet homogenates. Lymphocyte transformation studies are performed to assess cell mediated transplantation rejection phenomenon.

Manpower (in professional man years): .25/yr

Funding (in thousands) FY 77: 6.0

PROGRESS

Rat colonies of Lewis, Fischer and Wistar Furth have been established by the veterinary section of the CIS. The highly inbred Lewis strain has been demonstrated to accept isologous skin grafts as well as

WORK UNIT NO.: 76/301

PROGRESS - continued

pancreatic islet transplants successfully. Skin grafts from Fischer to Lewis also demonstrate no rejection phenomenon. Five Lewis to Lewis isologous pancreatic islet transplantations have been performed and no signs of rejection phenomenon have been observed as far as six months following the transplantation. nine transplantations of Wistar Furth to Lewis have been performed with rejection becoming apparent in a range of 1-5 days. Six Fischer to Lewis transplants have been performed with rejection being demonstrated at 1-5 days. With this control data as background islet cultures have been developed and it appears that pancreatic islet will survive the necessary conditions to perform transplantations of pancreatic islets following culturing at high oxygen tension in the absence of fetal calf serum. These studies are now in progress.

Immunological studies of the rejection phenomenon of autologous transplantation have indicated that diabetic Lewis animals have impaired cell mediated responses to islet antigen as assessed by lymphocyte transformation studies following islet transplantation. Normal animals given autologous islets such as Wistar Furth to Lewis demonstrate lymphocyte transformation 2-3 fold in excess of control animals not given autologous islets. Thus it appears immunologically that 14 days following pancreatic islet transplantation diabetic rat lymphocytes do not respond as vigorously as normal lymphocytes to islet antigen in vitro demonstrating the possibility of cell mediated responses and defects possibly involved in the rejection phenomenon. Because the rejection phenomenon occurs much earlier than 14 days, the studies are now being planned for earlier isolation of lymphocytes following transplantation.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Rosette Formation by T-Lymphocyte: I. Assay Method Using Primate Erythrocyte II. Assay Method Using Sheep Erythrocyte Treated with Neuraminidase.

WORK UNIT NO.: 76/302

PRINCIPAL INVESTIGATOR: George L. Brown, LTC, MSC, Ph.D.

ASSOCIATE INVESTIGATORS: Donald D. Paine, DAC, B.S.

OBJECTIVES

An evaluation of the rosette assay using primate erythrocytes and neurominidase treated sheep erythrocytes for human T-lymphocyte detection.

TECHNICAL APPROACH

Lymphocytes are isolated by Hypaque Ficoll sedimentation technique; T-lymphocyte population are evaluated with standard SRBC rosette test. Sheep erythrocytes are treated with neuraminidase and are tested for rosette formation in parallel with nontreated SRBC. Erythrocytes from Macaque nemestrina are studied for ability to form rosettes with human T-lymphocytes.

Manpower (in professional man years): 0.5/yr

Funding (in thousands) FY 77: 0.6

PROGRESS

Results of this study, based on test sensitivity, reproducibility, shelf life of erythrocyte storage and percentage of rosette formation, showed that the neuraminidase treated SRBC as the optimal system for the rosette test. Nonreproducible results, low counts, and decreased shelf life of erythrocytes were recorded with primate and nonneuraminidase-treated SRBC.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Effect of Physical Stress on the Cellular and Humoral Immune Mechanisms in Mice.

WORK UNIT NO.: 76/303

PRINCIPAL INVESTIGATOR: George L. Brown, LTC, MSC, Ph.D.

ASSOCIATE INVESTIGATOR: Joseph Lima, DAC, B.S.

OBJECTIVES

A study to evaluate the effects of maximum physical stress on mice during antigenic stimulation on immunoglobulin synthesis, lymphocyte transformation and secretion of antibody from splenic lymph node cells.

TECHNICAL APPROACH

The amount of physical stress, swimming, to the fatigue stage is determined. Prior to the study, all animals are swum (5 minutes) for one week for adaptation to shock. Animals comprising fatigued and not fatigued groups are immunized intravenously with SRBC in phosphate buffer saline. Anti-SRBC globulin is determined by direct hemoagglutination and passive hemoagglutination tests. Lymphoid cell element from splenic material is evaluated quantitatively and qualitatively for antibody germinal lymphoid cells. Representative splenic lymphocytic cell samplings at time intervals post immunization are stimulated with phytohemagglutin mitogen; lymphocyte transformation is assayed with tritiated thymidine uptake.

Manpower (in professional man years): 1.0/yr

Funding (in thousands) FY 77: 0.8

PROGRESS

Four groups of mice were evaluated post immunization with SRBC: (I) Control group; (II) Stressed group; (III) Antigenically stimulated non-stressed group; and (IV) Antigenically stimulated stressed group. Serum pools and splenic lymphoid cells representing samplings of primary

WORK UNIT NO.: 76/303

PROGRESS - continued

response were titered before and after treatment with 2-mercaptoethanol and for plaque assays, respectively. All animals were studied for splenic weight, body weight, and lymphocyte transformation post mitogenic stimulation. Results showed no significant differences in lymphocyte transformation to PHA in all groups studied (P = 0.52). Data on plaque antibody formation indicated a significant difference among all groups (P .005); greatest number of plaque-forming units seen on day 4 post immunization. There was no significant difference in body and spleen weights and anti-SRBC titers in fatigued vs. non-fatigued groups.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Calcium Metabolism in Diabetes Mellitus.

WORK UNIT NO.: 76/304

PRINCIPAL INVESTIGATOR: Art Charles, LTC, MC

ASSOCIATE INVESTIGATORS: Gary Treece, MAJ, MC
Fred Hofeldt, LTC, MC
PHil O'Barr, Ph.D., DAC
Marty Bassett, CPT, MC

OBJECTIVES

To determine if diabetes mellitus in humans is associated with renal unresponsiveness to parathyroid hormone. If this hypothesis is true, it could explain the bone demineralization asssociated with diabetes mellitus.

TECHNICAL APPROACH

Patients with diabetes but not on therapy will be assessed prior to being placed on therapy. If the assessment demonstrates no emergent need for diabetic control, the patient will be included into the study at which time the patient will be infused with thyroid hormone, and the patient's blood and urine will be analyzed for cyclic AMP in addition to other variable such as phosphate to prove or disprove whether diabetic kidneys are resistant to parathyroid hormone.

Manpower (in professional man years): .0/yr

Funding (in thousands) FY 77: .0

PROGRESS

To date no patients presenting to the hospital have been suitable for study.

Publications and Presentations. None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Standardization of Hypoglycemic Criteria using a Physiological Stimulus.

WORK UNIT NO.: 76/305

PRINCIPAL INVESTIGATOR: Art Charles, LTC, MC

ASSOCIATE INVESTIGATORS: Gary Treece, MAJ, MC
Fred Hofeldt, LTC, MC
Phil O'Barr, Ph.D., DAC

OBJECTIVES

To establish criteria defining normal postprandial blood glucose and glucoregulatory hormone concentrations following a test meal which provides more physiologic stimulus than pure glucose and to compare these data with the traditional oral glucose tolerance test. Also to observe whether patients thought to have idiopathic reactive hypoglycemia do in fact have low postprandial blood glucose on altered levels of glucoregulatory hormones associated with clinical findings following the test meal.

TECHNICAL APPROACH

Patients and normals will be given a test meal consisting of Figurines containing about a third of the daily caloric and protein carbohydrate and fat intake following which time multiple tests will be performed looking at glucose homeostasis.

Manpower (in professional man years): .10/yr

Funding (in thousands) FY 77: .05

PROGRESS

Eight patients presenting to the FAMC Endocrine Clinic with the tentative diagnosis of reactive hypoglycemia have been evaluated using glucose tolerance testing and Figurine tolerance testing. One patient previously classified as idiopathic reactive hypoglycemia following most recent tolerance test is clearly diabetic. The remainder of the patients studied have demonstrated symptoms following glucose tolerance tests

WORK UNIT NO.: 76/305

PROGRESS - continued

and sugars in the range considered diagnostic of reactive hypoglycemia associated with a rise of counter regulatory hormones eg HGH and cortisol. In every instance when the same patient is challenged with figurines the blood sugar does not decline and yet symptoms still occur unassociated with rises in counter regulatory hormones. These preliminary studies indicate that reactive hypoglycemia is an artifact of the oral glucose tolerance test and that the symptoms patients experience is unrelated to blood sugar.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Immunologic Disorders in Children and Adults: I. Correlation of Immune Functions in the Immunodeficiency State II. Correlation of Immune Functions of Leukemia and other Childhood Malignancies.

WORK UNIT NO.: 77/300

PRINCIPAL INVESTIGATORS: George L. Brown, LTC, MSC, Ph.D.
Donald G. Corby, COL, MC
James E. Shira, COL, MC
Richard D. deShazo, MAJ, MC

OBJECTIVES

Existing specialized immuno-chemical procedures will be consolidated into a registered protocol for use, on a consultative basis, by the hospital staff.

TECHNICAL APPROACH

A clinical laboratory immunology consultation service has been established. Main emphasis in performance and evaluation of specialized immuno-chemical tests, will be accumulation of scientific data, and laboratory facilities for training house-staff personnel. The major areas of studies include humoral and cellular immunity and leukocyte function evaluation. Patients are selected on the basis of seventy of recurrent infections, clinical immunodeficiency state, lack of response to medical management and availability for laboratory evaluations.

Manpower (in professional man years): 1.5/yr

Funding (in thousands) FY 77: 5.0

PROGRESS

A total of 161 patients consultative evaluations were performed. Of these, 153 were in the area of applied immunology (cellular & humoral) and 8 for special studies of abnormal hemoglobulins. The number of patients studied with indicated unusual findings were as follows: I. Hemoglobinopathy, Hb species described: 1 HbE, 1 HbAJ b bariant, 2 b thallasemia, 3 sickle cell. II. Applied immunology Serum protein profile evaluations: 28 cryoglobulinemias (20 IgG, 6 IgG-IgM, 2 IgG-IgM-IgA), 1 severe combined deficiency, 1 partial congenital Bruton's Syndrome, 1 Walderstrom's with polymerized IgM,

WORK UNIT NO.: 77/300

PROGRESS - continued

10 monoclonal (8 IgG, 2 IgA) gammopathies, 2 polyclonal gammopathies, 5 immunodeficiency (cellular), 2 myeloproliferative, 1 nephrotic syndrome. b. Applied serology: 2 patients evaluated for infertility using sperm immobilization test. c. Cellular immune evaluations: 70 patients, 200 evaluations; lymphocyte transformation post mitogenic stimulation (PHA, ConA, PWM) and SRBC rosette (T-lymphocyte).

Publications: None

Presentations:

Brown, G.L., Calcagno, J.V., Cromwell, R., Bennett, D.E., Tull, A.H., Spaulding, H.S. and W.A. Todd: Incidence of Group A Beta-Hemolytic Streptococcus in Healthy Children. Presented: American Society for Microbiology, New Orleans, Louisiana, May 1977.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Thyroglobulin Levels in Patients with Thyroid Carcinoma.

WORK UNIT NO: 77/301

PRINCIPAL INVESTIGATOR: Art Charles, LTC, MC

ASSOCIATE INVESTIGATORS: Phil O'Barr, Ph.D., DAC
Gary Treece, MAJ, MC
Fred Hofeldt, LTC, MC

OBJECTIVES

To determine if thyroglobulin serum levels reflect the occurrence of thyroid carcinoma metastases.

TECHNICAL APPROACH

The radioimmunoassay will be designed to measure serum circulating thyroglobulin levels in humans by isolating the thyroglobulin protein from human thyroid glands by column chromatographic techniques. Following the acquisition of pure human thyroglobulin the protein will be injected into rabbits on a pre-determined immunization schedule and rabbit serum will be harvested for analysis of anti-human thyroglobulin antibodies. Radioactive Iodine 125 thyroglobulin will be prepared by the chloramine T method. Following the development of the radioimmunoassay for serum thyroglobulin determination normals will be studied to determine normal circulating levels of serum thyroglobulin levels using the assays developed at FAMC. Patients will be studied in various stages of therapy following the diagnosis of thyroid carcinoma.

Manpower (in professional man years): .1/yr

Funding (in thousands) FY 77: 3.5

PROGRESS

The radioimmunoassay has been developed using human thyroglobulin as antigen that is sensitive to 1 ng/ml of circulating thyroglobulin. 65 normal volunteers have submitted specimens for analyses and the range of normal people is 3-45 ng/ml. Twenty patients with documented thyroid carcinoma have been evaluated for serum thyroglobulin levels and all patients with evidence of metastases studied

WORK UNIT NO.: 77/301

PROGRESS - continued

to date have values ranging from 1-12 ng/ml. Of extreme importance and previously unreported is the fact that two patients with local tumor metastases in the neck also have normal levels of 5 and 9 ng/ml. One patient with wide spread metastases has a value of 690 ng/ml.

Publications and Presentations: None

STATUS:

Ongoing.

OB-GYN

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Evaluation of "Pereyra-Harer" Procedure in Treating Urinary Stress Incontinence.

WORK UNIT NO.: 67/351

PRINCIPAL INVESTIGATOR: Keith F. Deubler, COL, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To evaluate the Pereyra method of urethro-vesical suspension as a means of treatment for patients with true urinary stress incontinence.

TECHNICAL APPROACH

This project is an attempt to define the long-term effect of one type of surgical repair for urinary stress incontinence in the female. Patients with urinary stress incontinence receive a complete urological work-up. The Bonney-Marchetti-Read "Stress test" is used to select surgical candidates. The chain cystogram is utilized as described by Green to define cases as Type I or Kennedy urethro-vesical plications as the primary surgical procedure used for control of Krantz procedure or a Pereyra-Harer procedure, depending on whether an abdominal or vaginal approach is indicated by the patient's other symptoms and findings. The long-term follow-up is done through the modality of patient questionnaire on a six-month basis. This will ultimately give sufficient data to define the relative merits of different surgical approaches in our treatment of this clinical problem.

Manpower (in professional man years): 0.3/yr

Funding (in thousands): FY 76 0
FY 77 0

WORK UNIT 67/351

PROGRESS

The project is continuing as outlined with accumulation of patients and follow-up information. There are currently over 200 patients in this study with approximately 90 of them being followed after a "Pereyra" procedure.

Publications: None

Presentations:

(1) Buffone, D.: Evaluation of the "Pereyra-Harer" Procedure in Treating Urinary Stress Incontinence. Presented: The Armed Forces District Meeting of the American College of OB-GYN, Las Vegas, Nevada, October 1970.

(2) Woods, W.M.: Evaluation of the "Pereyra-Harer" Procedure in the Treatment of Urinary Stress Incontinence. Accepted for Presentation. Armed Forces District Meeting of the American College of OB-GYN, Washington, D.C., November 1975.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Gynecologic Follow-up after Tubal Surgery for Sterilization.

WORK UNIT NO.: 73/353

PRINCIPAL INVESTIGATOR: Keith F. Deubler, COL, MC

ASSOCIATE INVESTIGATOR: Durell A. Hiller, CPT, MC
J.P. Elliott, CPT, MC

OBJECTIVES

1. To determine the incidence of GYN problems following tubal surgery for sterilization in a five-year postoperative follow-up.

2. To determine the failure rate of various types of tubal surgery for sterilization.

3. To determine complications (operative) of various types of tubal surgery for sterilization.

4. To determine morbidity (postoperative) from various types of tubal surgery for sterilization.

5. To determine patient's estimates of the value of the procedure.

TECHNICAL APPROACH

The long-term results of sterilization by tubal surgery as opposed to other means of sterilization will be evaluated by registering all these patients in the tumor registry and following their progress for several years by a questionnaire on a biannual basis.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 76: 0
FY 77: 0

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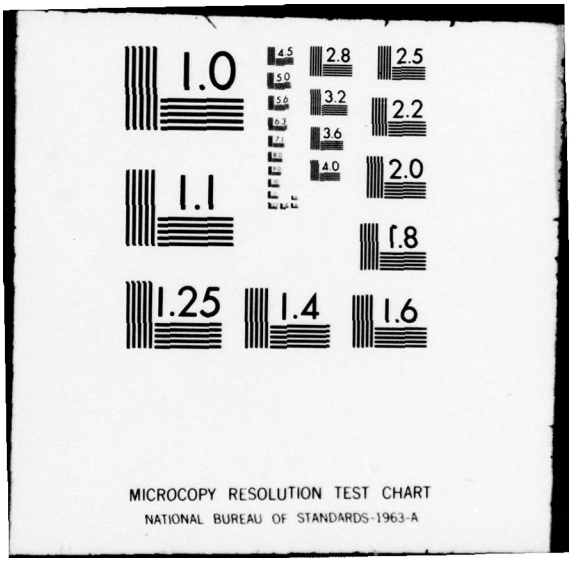
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WORK UNIT 73/353

PROGRESS

Data collection only, at present. Material collected has not been reviewed as yet. The three-year collection of cases is to be followed for five years and is to be maintained on these patients by questionnaire.

Publications: None

Presentations:

(1) Hiller, D.A., Elliott, J.P.: Tubal Ligation Syndrome Myth or Reality. Presented: Armed Forces Division of ACOG, New Orleans, Louisiana, October 1977.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: A Comparison of Oxytocin and Oral Prostaglandin E_2 in the Induction of Labor.

WORK UNIT NO.: 75/350

PRINCIPAL INVESTIGATOR: John P. Elliott, MAJ, MC

ASSOCIATE INVESTIGATOR: William P. Byars, Jr., CPT, MC

OBJECTIVES

To determine the effectiveness of Prostaglandin E_2 orally as an inducing drug in pregnancies which are to be terminated by medical means.

TECHNICAL APPROACH

Patients selected for induction of labor will be divided into two random groups which contain three subgroups each based on the Bishop's Score for evaluating ease of induction. Either oral Prostaglandin E_2 or intravenous oxytocin is administered until delivery or the method is termed failure after eight hours of no progress.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 76: 0
FY 77: 0

PROGRESS

Only two indicated inductions of labor have been performed at Fitzsimons Army Medical Center with Prostaglandin E_2, both for post-date pregnancies. One induction failed and one was successful. No maternal or infant morbidity was noted in either case. Due to the lack of success in establishing an elective induction program at Fitzsimons Army Medical Center, this project has been terminated as of 1 October 1977.

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Prevention of Radiation Induced Diarrhea.

WORK UNIT NO.: 75/351

PRINCIPAL INVESTIGATOR: Alfred S. Llorens, COL, MC

ASSOCIATE INVESTIGATOR: Robert Hesselgesser, MAJ, MC

OBJECTIVE

To determine if administration of aspirin to patients undergoing abdominal or pelvic radiation will influence gastrointestinal toxicity.

TECHNICAL APPROACH

A double-blind study will be carried out administering aspirin, .93 gm, daily and placebo to patients undergoing pelvic or abdominal radiation. Parameters to be evaluated are subjective assessment of gastrointestinal toxicity and also objective levels of prostaglandin F2α breakdown products.

Manpower (in professional man years): 0.2/yr

Funding (in thousands)	FY 76:	1.5
	FY 77:	2.5

PROGRESS

Although this protocol was unsuccessful it did ultimately result in the establishment of new RIA for prostaglandin F2α metabolites. This assay has proven valuable for other studies. The Principal Investigator (and Associate Investigator) of this study have departed this duty station and information pertaining to the project is not available.

Publications and Presentations: None

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: A Comparison of Serum Estriol Levels and Human Placenta Lactogen (HPL) Levels in the Management of Hypertensive and Vascular Disease in Pregnancy.

WORK UNIT NO.: 75/352

PRINCIPAL INVESTIGATOR: Keith F. Deubler, COL, MC

ASSOCIATE INVESTIGATOR: Thomas P. O'Barr, Ph.D., DAC

OBJECTIVES

The object of this study is to determine if HPL level obtained after the 30th week of gestation will be as effective in managing the outcome for mother and fetus as serum estriols which are currently being utilized at Fitzsimons Army Medical Center.

TECHNICAL APPROACH

During the 12 months from initiation of this study, all patients seen in the clinic or hospitalized with the diagnosis of hypertension in pregnancy, preeclampsia, glomerulonephritis, systemic lupus erythematosus, or other vascular diseases will be studied. Each patient will be studied from onset of clinical findings or 30 weeks' gestation until delivery.

Manpower (in professional man years): 0.25/yr

Funding (in thousands) FY 76: 2.5
FY 77: 2.5

PROGRESS

Preliminary evaluation of approximately 50 patients has been done. Results indicate the study should be continued to accumulate more data. Therefore the study is ongoing.

Publications: None

WORK UNIT NO.: 75/352

Presentations:

(1) Edward J. Lazarus, MAJ, MC, is presenting the preliminary results at the Annual Armed Forces Seminar and 16th Annual District Meeting, American College of Obstetrics and Gynecology, October 1977.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Evaluation of Ibuprofen (Motrin) in Dysmenorrhea.

WORK UNIT NO.: 76/350

PRINCIPAL INVESTIGATOR: William L. Black, MAJ, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To compare the relief of dysmenorrhea pain by Ibuprofen.

TECHNICAL APPROACH

Patients have been taken into the study and evaluated on either aspirin, placebo, or motrin for three consecutive cycles on each drug. The patients are filling our report cards with each cycle as to the amount of relief they have obtained and the amount of medication taken. These are returned after each set of three cycles and new drugs are obtained through the pharmacy.

Manpower (in professional man years): 0.1/yr

Funding (in thousands) FY 77: 0

PROGRESS

Since the onset of the study, there have been 15 women enrolled in the study out of the required 48 women. We have been able to have completion of the first cycle on medication for three women. Results are being held for tabulation at the end. The doctors in OB-GYN Clinic will refer any patients with continuous dysmenorrhea to the Principal Investigator in an attempt to get them on the protocol for the evaluation of this medication.

Publications and Presentations: None

STATUS:

Ongoing.

PEDIATRICS

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: The Effect of Positive Transpulmonary Pressure on Effective Pulmonary Blood Flow, Cardiac Output, Functional Residual Capacity, and Dynamic Pulmonary Compliance in Idiopathic Respiratory Distress Syndrome in Neonates.

WORK UNIT NO.: 73/413

PRINCIPAL INVESTIGATOR: William H. Parry, LTC, MC

ASSOCIATE INVESTIGATOR: Gerald B. Merenstein, LTC, MC

OBJECTIVES

Although positive transpulmonary pressure has been shown to be effective in the treatment of the idiopathic respiratory distress syndrome, few physiologic studies have been performed to delineate the reasons for its effectiveness. It is the purpose of this study to obtain data on various cardiopulmonary parameters in order to increase understanding of the physiologic effects of positive transpulmonary pressure in the neonate ill with the idiopathic respiratory distress syndrome.

TECHNICAL APPROACH

A noninvasive method utilizing the body plethysmograph will be utilized to gain information on various cardiopulmonary physiologic parameters both prior to institution of positive transpulmonary pressure and after institution of the technique.

Manpower (in professional man years): 0.2/yr

Funding (in thousands)		
	FY 76:	0
	FY 77:	0

PROGRESS

E.K. Motoyama has published a report on the determination for optimal continuous positive airway pressure for treatment of IRDS by measurement of esophageal pressure in the Journal of Pediatrics in September 1977.

WORK UNIT NO.: 73/413

PROGRESS - continued

Inasmuch as his data is similar to our preliminary data, the value of further investigational research into this problem seems limited. The equipment will continue to be used for clinical evaluation of pulmonary function in infants.

Publications and Presentations: None

STATUS:

Terminated.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Echocardiographic Assessment of Ventricular Size and Function in Infants of Diabetic Mothers.

WORK UNIT NO.: 75/400

PRINCIPAL INVESTIGATOR: G. B. Merenstein, LTC, MC

ASSOCIATE INVESTIGATOR: Gerald L. Way, MAJ, MC

OBJECTIVES

To determine serial dimensions of hearts of infants of diabetic mothers and to determine serial indices of myocardial contractility of hearts of infants of diabetic mothers.

TECHNICAL APPROACH

a. All LGA infants will be assessed, and those infants whose mothers satisfy White's Classification of Diabetes and Pregnancy will be evaluated.

b. Height, weight, and head circumference will be recorded.

c. Gestational age will be done according to Dubowitz exam within seventy-two hours, and a hematocrit will be obtained.

d. Left ventricular wall thickness and left ventricular internal dimensions will be measured from the echocardiograms and compared to normal newborns at this altitude. Left ventricular function will be determined by measuring velocity of circumferential fiber shortening.

Manpower (in professional man years): 0.2/yr

Funding (in thousands)		
	FY 76:	0
	FY 77:	0

PROGRESS

No additional patients have been admitted to the study since the report of 30 Jun 76. However, following the publication of the abstract in

WORK UNIT 75/400

Progress - continued

Pediatric Research and the presentation by MAJ Way at the American Academy of Pediatrics, the cardiomyopathy of infants of diabetic mothers has been reported by others and is now a well-recognized clinical syndrome in infants of diabetic mothers. For this reason, there is no further indication for continuing this project as a clinical investigation project.

Publications:

Way, G.L., Wolfe, R.R., Pettett, P.G., Merenstein, G.B., Simmons, M.A., Spangler, R.D., Nora, J.J.: Echocardiographic Assessment of Ventricular Dimensions in Myocardial Function in Infants of Diabetic Mothers, Pediatric Research 9:273, 1975 (Abst).

Presentations:

Way, G.: The Spectrum of Myocardiopathy in Infants of Diabetic Mothers. Annual Meeting of American Academy of Pediatrics, Cardiology Section, Washington, D.C., October 1975.

Status:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Effect of Prophylactic Antibiotic Therapy on Gravid Group B *Beta Hemolytic* Streptococcus Carriers.

WORK UNIT NO.: 75/401

PRINCIPAL INVESTIGATORS: Gerald B. Merenstein, LTC, MC
George L. Brown, LTC, MSC, Ph.D.

ASSOCIATE INVESTIGATOR: Ann H. Tull, B.S., DAC

OBJECTIVES

To evaluate several selective culture media for the isolation of Group B Beta Hemolytic Streptococcus (GBHS) and the use of prophylactic antibiotic therapy in antepartum GBHS carriers with regard to colonization of the infant.

TECHNICAL APPROACH

Endocervical cultures are obtained from all obstetrical patients at FAMC at the initial obstetrical visits and at delivery. Those positive are re-evaluated for GBHS at the 30th and 38th week visits. In addition, "positives" are placed in a control or a treatment group; those in the treatment group are placed on oral penicillin *or erythromycin, if allergic.* Ear, umbilical and cord cultures are obtained from each infant for GBHS evaluation. Numerous media incorporating inhibitory substances are evaluated for GBHS isolation. Isolated GBHS are studied for type specific antigen composition.

Manpower (in professional man years): 1.5/yr

Funding (in thousands) FY 76: 4.0
FY 77: 4.0

PROGRESS

Over a two-year period, 1,465 females and their progeny were screened for colonization with GBHS. One hundred sixty-eight (168) women (11.5%) and 55 infants (3.8%) were colonized. Fifty (50) women

WORK UNIT NO. 75/401

PROGRESS - continued

colonized with GBHS at 38-weeks gestation and their husbands were randomized to determine the value of antepartum oral antibiotic therapy in preventing infant colonization. Forty-four (44) women and their husbands completed the study. Analysis of the data indicated that a significant reduction in maternal ($p = 0.0008$) and infant ($p = 0.004$) colonization can be attained by oral antibiotic therapy. The use of prophylactic penicillin in gravid females colonized with GBHS at term is felt to have been demonstrated. The study has been temporarily halted while re-evaluation of the technique of evaluating mothers prior to term is studied.

Publications:

(1) Yost, C.C., Calcagno, J.V., Merenstein, G.B., Todd, W.A., Dashow, E.E., Brown, G.L., Tull, A.H., and Kile, D.E.: Group B Beta Hemolytic Streptococcus: Improved Culture Detection and a Controlled Treatment Trial. Clinical Research, 24:186A, 1976.

Presentations:

(1) Calcagno, J.V., Brown, G.L., Tull, A.H., Yost, C.C., Jolly, D.J., and Cromwell, R.K.: Evaluation of Three Collection - Transport Systems for the Isolation of Group B Streptococcus from Pre-Partum Women and Neonates: American Society for Microbiology, Atlantic City, New Jersey, 1976.

(2) Luzier, T.L.: The Treatment of Gravid Females at Term Colonized with Group B Beta Hemolytic Streptococcus: A Randomized Study. Accepted for presentation Military Section, American Academy of Pediatrics, November 1977.

(3) Luzier, T.L.: The Treatment of Gravid Females at Term Colonized with Group B Beta Hemolytic Streptococcus: A Randomized Study. Second prize Hugh Mahon Award, Fitzsimons Army Medical Center, Denver, Colorado, June 1977.

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Early Digitalization in Premature Infants with Idiopathic Respiratory Distress (IRDS) Who Have Echocardiographic Evidence of Left Atrial Enlargement.

WORK UNIT NO.: 75/402

PRINCIPAL INVESTIGATOR: Gerald L. Way, MAJ, MC

ASSOCIATE INVESTIGATORS: Gerald B. Merenstein, LTC, MC
John R. Pierce, MAJ, MC

OBJECTIVES

To determine the usefulness of early digitalization in altering the progression of congestive heart failure and left-to-right shunting through the PDA in premature infants with IRDS.

TECHNICAL APPROACH

Infants with RDS and left atrial aortic diameter ratio of greater than 1.0 by echocardiograph will be included in the two study groups. The two study groups will be Group A-infants who will be digitalized with 40 mcg/kg dose of digoxin and maintained at 10 mcg/kg/day. Group B-infants who will not receive digoxin unless they clinically demonstrate overt congestive heart failure. Echocardiograms will be repeated every other day throughout the respirator course, and subsequently only if abnormal findings remain. Additional echocardiograms will be obtained if the clinical situation deteriorates. Echocardiograms will be evaluated with coinciding arterial blood gases, chest x-rays, EKG's, and laboratory data which will be done as needed for clinical management.

Manpower (in professional man years): .25/yr

Funding (in thousands) FY 77: 1.0

PROGRESS

Patients who were originally evaluated with echocardiography, however, who were not entered in the project as such at the time because of awaiting authorization from Washington, have been evaluated with

WORK UNIT NO.: 75/402

PROGRESS - continued

reference to fluid intake and evidence of left-to-right shunting. This retrospective evaluation using echocardiographic evidence of left-to-right shunting has revealed significant increase in babies with left-to-right shunting who received generally accepted daily fluid administration as opposed to those babies who had been fluid restricted. This data has been tabulated and has been submitted for publication by Dr. Stephen M. Golden. In terms of the study itself as proposed at the time of changeover in July when new residents arrived, part of our data has been misplaced, and the data are presently being retrieved. At the time the data were misplaced, we had approximately 8 patients in each randomized group, and at the time were getting ready to analyze the data statistically to see if there was any significance between the digitalized group and the non-digitalized group. It appeared that there was no effect of digoxin administration early on the final outcome of the baby.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Evaluation of High Intensity Fiberoptic Transillumination in Infants.

WORK UNIT NO.: 76/400

PRINCIPAL INVESTIGATOR: Stephen M. Golden, LCDR, MC

ASSOCIATE INVESTIGATORS: Gerard Breitzer, CPT, MC
Gerald B. Merenstein, LTC, MC

OBJECTIVES

To establish a new set of normal values of transillumination distances of infants' skulls using a 5,000 foot-candle fiberoptic light; to determine the efficacy of high intensity light in diagnosing pneumothoraces.

TECHNICAL APPROACH

All children in the normal newborn nursery and pediatric outpatient clinic and well child clinics for routine visits will have their skulls transilluminated using 3,000, 4,000, and 5,000 foot-candles of light from a fiberoptic source. Areas transilluminated will be the anterior fontanelle, posterior fontanelle, left parietal bone above the pinna midway on a line from the external air canal to the left eye on the frontal bone. Measurements of transillumination will be made from the center of the beam as outlined by Cheldelin et al. and will be compared with previous study results. Infants in the nursery with respiratory distress will be examined using the fiberoptic light as discussed by Kuhns, et al. to see if a pneumothorax or pneumomediastinum can be diagnosed by transillumination.

Manpower (in professional man years): 0.2/yr

Funding (in thousands) FY 77: 0

PROGRESS

Forty (40) patients were admitted to the study, and after permits were obtained, studied by the principal investigator. With the completion of the principal investigator's training and his reassignment, an additional investigator, Dr. Breitzer, has been

WORK UNIT NO.: 76/400

PROGRESS - continued

added and will continue the project over the next several months.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Laboratory Diagnosis of Neonatal Sepsis.

WORK UNIT NO.: 77/400

PRINCIPAL INVESTIGATOR: Edward N. Squire, Jr., CPT, MC

ASSOCIATE INVESTIGATORS: Harvey Reich, MAJ, MC
Gerald B. Merenstein, LTC, MC

OBJECTIVES

To quantitate sensitivity, specificity, and predictive value of laboratory tests used in the evaluation of neonatal sepsis and infection.

TECHNICAL APPROACH

The study group is to consist of approximately 20 culture-proven cases of sepsis and 20 controls. Controls are proven by negative cultures and no recurrence of symptoms, with antibiotics having been discontinued after a 3-day course. Sepsis work-ups on the newborn will consist of tests currently recommended in the literature as being valid tools in the diagnosis of neonatal sepsis. These will include CBC and differential, appropriate cultures and x-rays, mini sed rate, and consideration of C-reactive protein and IgM in some infants. Since all of the laboratory tests done are currently recommended in the normal clinical evaluation and treatment of neonates, and no additional blood is being drawn, no permits for research protocol will be obtained from the parents. The protocol is designed to observe and evaluate current techniques utilized for the diagnosis of neonatal sepsis.

Manpower (in professional man years): 0.2/yr

Funding (in thousands) FY 77: 6.0

PROGRESS

In cooperation with the Newborn Center at Denver Children's Hospital, sufficient patients have been entered into the study, so that no

WORK UNIT NO.: 77/400

PROGRESS - continued

further patients will be evaluated. The data is currently being evaluated.

Publications: None

Presentations:

Squire, E.N., Jr.: Neonatal Sepsis, presented 12th Annual Uniformed Services Pediatric Seminar, El Paso, Texas, March 1977.

STATUS:

Completed.

PATHOLOGY

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: The Relationship of Estrogenic Hormones to the Coagulation Balance.

WORK UNIT NO.: 71/450

PRINCIPAL INVESTIGATOR: Paul W. Holley, MAJ, MC

ASSOCIATE INVESTIGATORS: James J. Bergin, COL, MC
Donald G. Corby, COL, MC

OBJECTIVES

The objective is to continue to investigate the changes in the natural inhibitor mechanisms of coagulation brought about by female sex hormones; i.e., estrogens and combined progesterone-estrogen oral contraceptives. The main purpose for such investigation is to determine whether prospective application of the thrombin generation and anti-thrombin-III tests, either alone or with other clotting parameters, can define those patients taking exogenous hormones who would be at increased risk of developing thrombovascular disease.

TECHNICAL APPROACH

The approach is twofold: (1) To study the relationship of the two parameters to each other by various assay techniques with several different plasma and serum fractions in order to insure that they are indeed independent parameters and not mutually dependent upon each other, and (2) to study large numbers of women in various categories while they are symptomatic and asymtomatic to confirm that the tests have prognostic value, or to disprove their usefulness for this purpose.

Manpower (in professional man years): 2.0/yr

Funding (in thousands) FY 76: 5.0
FY 77: 0.0

WORK UNIT NO.: 71/450

PROGRESS

Due to the resignation of the principal investigator no further work was done on this study.

Publications:

(1) Zuck, T. F., Bergin, J. J., and Raymond, J. M.: Implications of Depressed Antithrombin III Association with Oral Contraceptives. Surg. Gynec. & Obstet. 133:209, 1971.

(2) Zuck, T. F., and Bergin, J. J.: Thrombotic Predisposition Associated with Oral Contraceptives. Obstet. & Gynec. 41:427, 1973.

(3) Zuck, T. F., Bergin, J. J., and Raymond, et al.: Platelet Adhesiveness in Symptomatic Women Taking Oral Contraceptives. Thromb. Diath. Hemorr. 26:426, 1971.

(4) Zuck, T. F., Bergin, J. J., and Perkins, R. P.: Antithrombin III Activity and Oestrogen Content of Oral Contraceptives. Lancet 1:831, 1973.

(5) Holley, P. W., Bergin, J. J., Powers, J. S., Barber, J. A., Rush, P. A., and Zuck, T. F.: Antithrombin-III Depression in Response to Estrogen Dose in Oral Contraceptives. (In preparation for publication).

(6) Bergin, J. J., Holley, P. W., Dobbs, R. M., Barber, J. A., and Rush, P. A.: Depression of Antithrombin-III in Patients with Prostatic Carcinoma Receiving Estrogen Therapy. (In preparation for publication).

(7) Holley, P. W., Bergin, J. J., Barber, J. A., Rush, P. A., and Zuck, T. F.: Alteration of Thrombin Generation and Antithrombin-III Level with Respect to Dose of Conjugated Equine Estrogens. (In preparation for publication).

Presentations:

(1) Zuck, T. F.: Rates of Generation and Progressive Neutralization of Thrombin in Symptomatic Women Taking Oral Contraceptives. Presented: II Congress, International Society on Thrombosis and Haemostasis, Oslo, Norway, 1971 (Abs., P. 106).

WORK UNIT NO.: 71/450

Presentations - continued

(2) Zuck, T. F.: Shifts in Thrombin Kinetics Induced by Conjugated Equine Estrogens. Presented: III Congress, International Society on Thrombosis and Haemostasis, Washington, D.C., 1973, (Abs., P. 160).

(3) Zuck, T. F.: On the Mechanism of Antithrombin III Depression in Women Using Oral Contraceptives. Presented: IV Congress, International Society on Thrombosis and Haemostasis, Vienna, Austria, 1973, (Abs., P. 223).

(4) Zuck, T. F.: Thrombin Generation Index and Antithrombin III as Guides to Anticoagulation in the Surgical Patient. Presented: Regional Meeting of American College of Physicians, Steamboat Springs, Colorado, 1974.

(5) Zuck, T. F.: The Pill and Thromboembolic Disease. Presented: Colorado Heart Association, Snowmass-at-Aspen, Colorado, 1974.

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Treatment of Hemophilia A or B with Inhibitors Using Auto-Factor IX Concentrate (Human).

WORK UNIT NO.: 75/450

PRINCIPAL INVESTIGATOR: Paul W. Holley, MAJ, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

To evaluate treatment of hemorrhagic episodes in Factor VIII or IX deficient patients with inhibitor activity using the activated prothrombin complex concentrate Auto-Factor IX Concentrate (Human).

TECHNICAL APPROACH

Hemophilia A or B patients with inhibitor activity requiring treatment for significant hemorrhage will be evaluated clinically and with laboratory coagulation testing (APTT, PT, platelet count, fibrinogen, FDP, Factor VIII activity) prior to and after treatment with Auto-Factor IX Concentrate.

Manpower (in professional man years): 0

Funding (in thousands) FY 76: 0
FY 77: 0

PROGRESS

Due to the resignation of the principal investigator the study is terminated.

Publications and Presentations: None

STATUS:

Terminated.

DENTISTRY

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Clinical Procedures Which Cause Implantation of Impression Materials.

WORK UNIT NO.: 76/550

PRINCIPAL INVESTIGATOR: Bruce J. Zimmerman, MAJ, DC

ASSOCIATE INVESTIGATOR: Arthur G. Clifford, COL, DC

OBJECTIVES

To determine which commonly used clinical procedures predispose to unintentional subepithelial implantation of rubber base impression material.

TECHNICAL APPROACH

Mongrel dogs weighing about 30 kilograms will be anesthetized utilizing light general anesthesia. Mandibular premolar teeth will be prepared for full veneer crowns utilizing standardized techniques which are commonly used for routine preparations of human teeth. Two to six teeth will be prepared on each dog. One side of the mandible will serve as the control, the other side will be the experimental side. Three criteria will be evaluated to determine if they substantially increase the possibility of unintentionally embedding rubber base impression material into subepithelial tissues. These criteria will be evaluated singly and in combination: (1) The effect of electrosurgery; (2) The effect of different air syringe pressures and orifices; (3) The effect of retraction cord with and without an astringent (Aluminum Sulfate). The selected sites of the mandible will be radiographed prior to and immediately following the operation. After the final radiographs are made, the mandible will be sectioned using a Stryker saw and the entire operative site including three teeth will be removed. The control side will also be sectioned. The gross specimens will then be submitted to Pathology for demineralization, staining, sectioning and mounting. The slides will be examined by the investigators to determine the amount and exact location of any embedded impression material. The animals will be sacrificed before the removal of the block sections of the mandible.

Manpower (in professional man years): 0.25/yr

Funding (in thousands)		
	FY 76:	2.0
	FY 77:	0.0

WORK UNIT NO.: 76/550

PROGRESS

Principal investigator has departed this station. He indicated that he would mail in a report concerning the completed project to the Clinical Investigation Service, Fitzsimons Army Medical Center.

Publications and Presentations: None

STATUS:

Completed.

RADIOLOGY

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Scintigraphic Evaluation of Thyroid Disorders - Clinical Evaluation of Oral ^{123}I Sodium Iodide.

WORK UNIT NO: 73/600

PRINCIPAL INVESTIGATOR: Nasser Ghaed, LTC, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

Clinical evaluation of ^{123}I Sodium Iodide for oral administration supplied by Medi-Physics, Inc.

TECHNICAL APPROACH

One to four capsules (100 to 400 uCi) of ^{123}I-Sodium Iodide Capsules will be administered orally to patients suspected of having thyroid disease. Measurement of ^{123}I accumulation in thyroid and thyroid scintigraphy will be performed at varying time intervals. The number of subjects with known or suspected thyroid disease will be unlimited and there will be no limitation on sex or age of patients. Data obtained will be recorded on either the special patient report forms provided or in the routine fashion used to record radioiodine studies of the thyroid in the laboratory of the investigator. The quality of the scintigraphic images of the thyroid and the radioiodine accumulation in the gland will be evaluated and compared with that obtained using other agents previously employed by the investigator for this purpose. Adverse reactions will be reported immediately to Medi-Physics, Inc. Reports of clinical studies will be made periodically to Medi-Physics, Inc. and to appropriate state licensing agencies where applicable. Clinical evaluation of these agents as described above is considered adequate since the use of radioiodine for evaluating thyroid function and morphology is well established and the detailed studies of changes in in vivo distribution of these materials with time in human subjects is well documented in the medical literature.

WORK UNIT 73/600

TECHNICAL APPROACH - continued

Manpower (in professional man years): 0.5/yr

Funding (in thousands) FY 76: 0
FY 77: 0

PROGRESS

One hundred and sixty-nine studies using I-123 (Sodium Iodide) for evaluation of patients suspected of having thyroid disease. The I-123 studies were resumed as of 30 June 1976.

Publications and Presentations: None

STATUS:

Completed.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Bone Marrow Scintigraphy and Scintigraphic Localization of Soft Tissue Tumors by Use of Indium-111 Chloride

WORK UNIT NO.: 74/600

PRINCIPAL INVESTIGATOR: Nasser Ghaed, LTC, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

Clinical evaluation of Indium-111 Chloride supplied by Medi-Physics, Inc. The evaluation of the agent is significant in that it represents a method of studying sites of erythropoiesis in bone marrow and allows scintigraphic localization of soft tissue tumors by non-invasive techniques. In selected patients, this affords clinical information which could not be obtained by other methods.

TECHNICAL APPROACH

Up to 2mc of Indium-111 Chloride or proportionally less depending on body weight supplied by Medi-Physics, Inc. will be administered intravenously to patients referred to Nuclear Medicine Laboratory for either scintigraphic evaluation of sites of erythropoiesis in bone marrow or the presence of soft tissue tumors. After administration routine scintigraphic procedures with conventional equipment for periods up to 96 hours depending on the patient's clinical situation will be peformed. The number of subjects with known or suspected hematologic disease will be unlimited and there will be no limitation on sex or the age of patients. Radionuclide will not be administered to pregnant patients or patients under the age of 18 unless the clinical situation is severely dependent upon this study. Data obtained will be recorded in the routine fashion used to record radionuclide studies. This consists of a consultation sheet from the referring physician which will be appropriately answered. Selective scans will be copied on polaroid film included with the record and returned to the patient's chart. The quality of the scintigraphic images of the bone marrow and tumor site will be evaluated so the best image is obtained. Adverse reactions will be reported immediately to Medi-Physics, Inc. and to appropriate state license and agencies where

WORK UNIT 74/600

TECHNICAL APPROACH- continued

applicable. Clinical evaluation of these agents as described above is considered adequate since the use of Indium-111 Chloride is a substitute for iron and is well established in the literature.

Manpower (in professional man years): 0.05/yr

Funding (in thousands) FY 76: 0
FY 77: 0

PROGRESS

Patients have now become available, and there have been three Indium-111 Chloride studies to date.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Use of Gallium 67 Citrate in Evaluation of Patients with Known or Suspected Tumors and Pyogenic Abscesses.

WORK UNIT NO.: 74/601

PRINCIPAL INVESTIGATOR: Nasser Ghaed, LTC, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

Clinical evaluation of Gallium 67 Citrate supplied by Medi-Physics, Inc.

TECHNICAL APPROACH

The evaluation of this agent is significant in that it represents a method of diagnosing tumors that cannot be visualized by other conventional means, resulting in significantly more information on each patient with initial diagnosis, initial therapy and follow-up care. It will be used to localize pyogenic abscesses primarily subdiaphragmatic abscesses which cannot be localized by conventional methods. Use of this agent will enhance the diagnosis of this serious medical condition and ultimate treatment of the patient.

Manpower (in professional man years): 0.5/yr

Funding (in thousands) FY 76: 0
FY 77: 0

PROGRESS

Twenty-two studies using Gallium 67 Citrate for evaluation of patients with known or suspected tumors or pyogenic abscesses have been completed. The radiopharmaceutical proved adequate for the intended diagnostic purpose and again no detectable side effects were observed.

Publications and Presentations: None

STATUS:

Ongoing.

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: The Use of Indium 111 DTPA for the Study of Cerebrospinal Fluid Pathways.

WORK UNIT NO.: 74/602

PRINCIPAL INVESTIGATOR: Nasser Ghaed, LTC, MC

ASSOCIATE INVESTIGATOR: None

OBJECTIVES

Clinical evaluation of Indium 111 DTPA in aqueous ionic solution (pH 7 to 8) for study of cerebrospinal fluid pathways as supplied by Medi-Physics, Inc.

TECHNICAL APPROACH

Evaluation of this agent represents a method of studying cerebrospinal fluid pathways in selected patients with a compound that will result in significantly less absorbed radiation doses to patients than the methods currently used. The incidence of side reactions, such as fever, headaches and mild meningitis, will probably be decreased in comparison to the compound presently used.

Manpower (in professional man hours): 0.1/yr

Funding (in thousands) FY 76: 0
FY 77: 0

PROGRESS

Five studies using Indium 111 DTPA for evaluation of patients with cerebral spinal fluid pathways pathology have been completed. The radiopharmaceutical proved adequate for the intended diagnostic purpose, and again no detectable side effects were observed.

Publications and Presentations: None

STATUS:

Ongoing.

HOSPITAL CLINICS

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: Establishment of and Training in Methods for Special Studies of Abnormal Hemoglobins.

WORK UNIT NO.: 74/651

PRINCIPAL INVESTIGATOR: Nicholas C. Bethlenfalvay, COL, MC

ASSOCIATE INVESTIGATOR: George L. Brown, LTC, MSC
Donald G. Corby, COL, MC

OBJECTIVES

To establish and conduct training in methods for special studies of abnormal hemoglobins.

TECHNICAL APPROACH

Plans are to familiarize existing personnel in the performance of procedures involving biochemical study of hemoproteins using existing equipment.

Clinical studies of mutant human and animal hemoglobins have defined the effects of molecular aberrations on physiologic processes. Amino acid substitutions or deletions in the alpha, beta, gamma and delta chains dictate a variety of structural alterations which may modify hemoglobin affinity for oxygen, or affect the stability of the hemoglobin molecule. A laboratory to aid the clinician or researcher in his investigation of a mutant hemoglobin is not available in the Denver Metropolitan area. A thorough preliminary special investigation of hemoglobins almost always kindles the interest and support of established investigators in CONUS or abroad, where amino acid analyses in the end ultimately reveal the molecular lesion.

Manpower (in professional man years): 0.2/yr

Funding (in thousands) FY 76: 2.5
FY 77: 2.5

WORK UNIT 74/651

PROGRESS

The following procedures can now be performed: Preparation and preservation and storage of hemoglobin and globin. Zone electrophoresis of hemoglobin in various media and electrophoresis in polyacrylamide gel with isoelectric focusing. Quantitation of Hb F. Quantitation of Hb A_2 by microcromatography. Hb stability testing by the isopropanol technique. Electrophoresis of urea dissociated globin, and qualitative and quantitative recovery of hemoglobin and its subunits using column chromatography.

Since 30 June 1975 the following in new methodology was acquired: Hybridization procedures to delineate alpha vs. beta chain variant hemoglobins. Separation of hemoglobins into alpha and beta chains by reaction with PMB or PCMB. Globin chain synthesis studies using either ^{3}H leucine or ^{14}C leucine have commenced and, at this stage are aimed at establishing a range of normal control values. The following cases are currently being investigated including globin chain synthesis studies: (1) Hemoglobin Lepore - Boston, and (2) A large family (6 members) with alpha Thalassemia (HG H disease).

Publications and Presentations: None

STATUS:

Ongoing.

NURSING

CLINICAL INVESTIGATION SERVICE
FITZSIMONS ARMY MEDICAL CENTER
Denver, Colorado 80240

RESEARCH PROJECT RESUME
30 SEP 77

TITLE: The Impact of Pediatric Nurse Practitioner Programs: An Exploratory Methodology Study.

WORK UNIT NO.: 75/700

PRINCIPAL INVESTIGATOR: American Nurses' Association, Inc.

ASSOCIATE INVESTIGATOR: Marian J. I. Walls, LTC, ANC

OBJECTIVES

(1) To select a representative sample of pediatric nurse practitioner programs to be included in the study based upon selected program characteristics and a listed universe of goals.

(2) To operationalize the universe of goals for pediatric nurse practitioner programs.

(3) To determine congruence between goals of selected PNP programs and their curricula utilizing the criteria of emphasis and thoroughness.

TECHNICAL APPROACH

Much of the study had been curtailed due to lack of funding. The only aspect will be the collection of data and involves questionnaires which will be completed by program directors.

Manpower - N/A

Funding - The American Nurses' Association.

PROGRESS

Questionnaires were completed by Course Director, May 1976. The study was completed December 1976.

Publications:

Taunton, R.L., Sakumura, J.S., and Soptick, J.M.: Implementations of Goals in the Curricula of a Sample of Pediatric Nurse Practitioner/ Associate Programs. American Nurses' Association, Inc., 1976.

Presentations: None

STATUS:

Completed.

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